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ADDENDA

It is regretted that the following entries were omitted from the index to Vol. 61. Please insert them in the appropriate places:

AUTHORS

Johnstone, R. W., *see* Kerr, J. M. M.
Kerr, J. M. M., Johnstone, R. W., and Phillips, M. H. (ed.). *Historical review of British obstetrics and gynaecology, 1800–1950* (Review), 708
Phillips, M. H., *see* Kerr, J. M. M.
Schauffler, G. C. *Paediatric gynaecology* (Review), 707

SUBJECTS

Book reviews:
Kerr, Johnstone and Phillips (ed.): *Historical review of British obstetrics and gynaecology, 1800–1950*, 708
Schauffler: *Paediatric gynaecology*, 707

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A NEW MULTICHANNEL EXTERNAL TOCOGRAPH

BY
MOSTYN P. EMBREY, B.Sc., M.D., F.R.C.S., M.R.C.O.G.
First Assistant
Nuffield Department of Obstetrics and Gynaecology, University of Oxford

A FUNDAMENTAL difficulty in the elucidation of the problems of abnormal uterine action is that of satisfactorily recording and assessing uterine motility, and it is natural that many experimental investigations have been directed to this end. The earlier attempts at obtaining a graphic record of uterine contractions have been reviewed elsewhere (Embrey, 1940; Murphy, 1947) and need not be detailed, but briefly such recording may be by internal or external means.

Internal Tocography. This has mostly been effected by the introduction of a hydrostatic balloon or metreurynter between the membranes and the uterine wall connected with a pressure recording apparatus. The method has been much used and to good purpose by Bourne and Burn (1927) and Moir (1932, 1935), whose works in this connexion are well known. It enables changes in uterine pressure to be accurately recorded and is applicable not only in labour but it can be adapted for use in the puerperium.

More recently changes in intra-uterine pressure have been recorded by directly tapping the amniotic sac—which is itself the intra-uterine balloon—and connecting it to a manometer. Alvarez and Caldeyro (1950) achieved this by abdominal paracentesis, while Williams and Stallworthy (1952) punctured the amniotic sac *per vaginam*. A disadvantage of these methods is that they can only be employed during or immediately preceding labour.

External Tocography. The recording of uterine contractility by an apparatus applied to the maternal abdomen is of course indirect and cannot quantitatively measure uterine pressure, but it has the advantage that there is no trespass of the genital canal and so avoids the inherent objection of internal recording.

External tocographs have been of several types. In Dodek's apparatus (1932) movements of a plunger applied to the abdomen were transmitted to a recording tambour by a pneumatic system. Moir (1935) used a modification of this apparatus in which the method of recording was hydraulic, and similar apparatus has been employed by the writer.

In recent years mechanical and mechano-electrical recorders have received more attention. Murphy's (1947) publications have popularized the Lorand tocograph. This is a mechanical clockwork instrument, in which the actuating plunger projects a fixed distance from its base. Using it Murphy claims to estimate uterine tone as well as contractions and distinguishes hypertonic and hypotonic types of uterine activity.

The multichannel strain gauge tokodynamometer of Reynolds, Heard, Bruns, and Hellmann (1948), and Reynolds, Hellmann and Bruns (1948) employs a mechano-electrical device. A non-adjustable plunger actuates a strain gauge and by suitable electronic magnification produces a graphic record. Three strain gauges enable the activity of different parts of the uterus to be studied simultaneously. The apparatus is necessarily both complicated and costly; but it has been used by Reynolds with good effect, and from this work he has derived his concept of coordinated uterine activity with a "gradient of activity" and "fundal dominance".

The recording of uterine contractions by measuring changes in electrical potential (Dill and

Maiden, 1946) has not so far been very fruitful.

The disadvantage of internal tocography—apart from the objection of mechanical stimulation of uterine activity—is that the introduction of any instrument into the uterus requires a quite elaborate surgical technique if the risk of infection is to be avoided. Anaesthesia may be needed and the necessary intrusion of the birth canal must be disturbing to the patient, may be objected to, and will frequently be contra-indicated by the clinical circumstances of the case. The method is obviously not suitable for all cases and, at the best, numerous opportunities for study will be lost. In contrast, external recording is equally suitable in pregnancy, all stages of labour and the puerperium and, providing it achieves the accuracy of the internal method, external tocography has clear advantages in any large scale study of uterine action as a simple method applicable in all circumstances.

With these points in mind and with some experience of, and dissatisfaction with, various known internal and external methods of recording, the author has experimented with several types of apparatus, the aim always being to produce a simple yet efficient, robust, external tocograph, easily operated, requiring little supervision and capable of recording uterine contractions in all cases. These requirements have been fulfilled in the multichannel external tocograph now to be described.

A New Multichannel External Tocograph

Developed as a 3-channel instrument (Fig. 1) the method of recording adopted—after experiment with several alternatives—uses a hydraulic system. Each actuating head of the tocograph incorporates a "Hydroflex" metal bellows of suitable characteristics. This is connected by protected polythene tubing to a twin "Hydroflex" bellows in the recording head which moves a pen, the latter being pre-set, requiring no adjustment to paper and having a continuous ink feed. The fluid linkage is sealed at manufacture and requires no attention. The recorder measures 12×7×4 inches and contains a synchronous electric motor which drives a roll of paper 5¾ inches wide, moving at the rate of 0·2 inches per minute approximately and giving more than 48-hours continuous recording. A time marker is incorporated.

The actuating head has a circular base ring 3 inches in diameter which is applied to the maternal abdomen, being held in place by an adjustable elastic band. Contraction of the uterus causes an upward deflection of the contact plunger which is transmitted to the "Hydroflex" bellows and, by fluid pressure, faithfully relayed to the recording bellows. The recording is linear, and, by suitably choosing the elasticity characteristics of the bellows, an instrument has been evolved which is both sensitive and accurate but without the "temperament" of an experimental apparatus.

It is to be emphasized that this tocograph requires the minimum of attention in use—the actuating head has only to be applied to the abdomen and the recorder produces a graphic record at the turn of an "on-off" switch, without adjustment to paper, pen, ink-supply or hydraulic linkage. The only adjustment—and this is an important provision—is in the actuating head, where the contact plunger has a range of vertical movement controlled by a thumb screw.

The Tocograph in Use

During uterine contractions there is (1) anterior displacement of the uterus and consequent increase of the antero-posterior diameters of the abdomen, and (2) palpable hardening of the uterus. The first of these factors is variable and, while it is appreciated to some extent, it is probable that the external tocograph also records the hardening of the uterus, for uterine contractions can be satisfactorily recorded by a tocograph which rides freely on the abdomen and records can be obtained even in the puerperium.

In operation, the contact plunger of the tocograph indents the abdominal wall and also to some extent the relaxed uterus, and its subsequent upward displacement is proportional to any uterine contraction and hardening. The indentation of the relaxed uterus produced by a constant force applied to the plunger under standard conditions could be assumed to be a measure of tone of the organ were it not for the interposition of the abdominal wall. It is on this assumption that Murphy bases his observations

FIG. 1

The multichannel external tocograph. Inset: the actuating head.

of uterine tone, but the author makes no claim to measure uterine tone in this way. Rather has it been observed that, in any recorder in which the plunger projects a fixed distance, both the "tone" and the character of the contraction pattern are partly dependent on the thickness of the abdominal parieties, and that in a stout patient satisfactory tracings cannot always be obtained. But the provision of an adjustable contact plunger, which can be advanced into the abdominal wall, overcomes this latter difficulty and enables contractions to be picked up and recorded in all cases. At the same time estimation of the "tone" of the parieties—if desired—is not prevented.

The most interesting contributions to external tocography have been made by Reynolds *et al.* Stressing the importance of a gradient of uterine activity from fundus to cervix with fundal dominance, his observations with the Toko-dynamometer are in accord with the conception that inefficiency of the expulsive forces is mostly the result of incoordinate uterine action. The simpler multichannel external tocograph now described also permits detailed study of the contraction pattern of uterine activity. Work, so

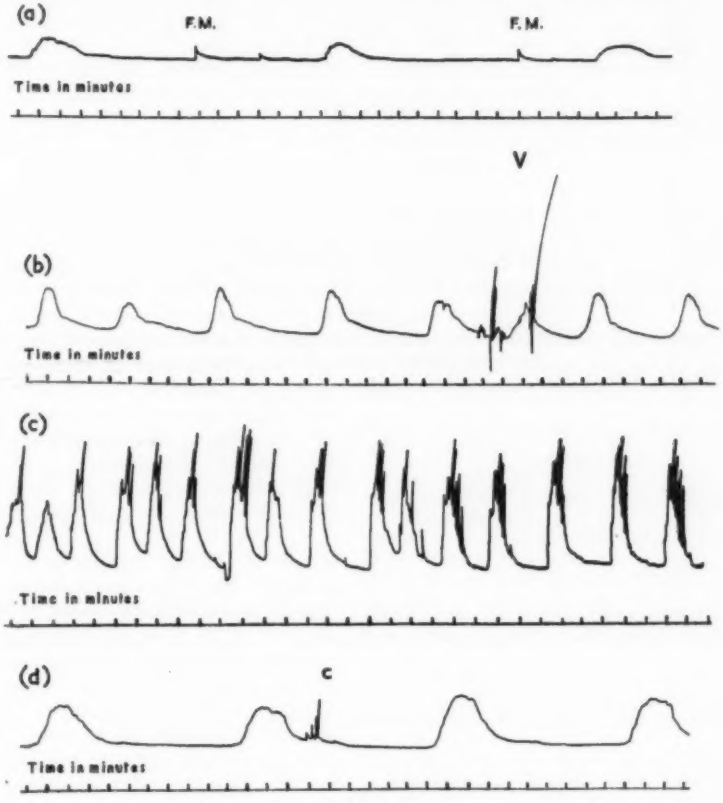

FIG. 2

The characteristics of normal uterine activity in (a) pregnancy (39th week), (b) labour 1st stage, (c) labour 2nd stage and (d) puerperium 2nd day. (F.M.: Foetal movements. V: Vomiting. C: Coughing.)

far, while substantiating some, has not corroborated all Reynolds's observations, but these are matters which it is hoped to deal with in a separate communication.

Representative Records

The known characteristics of uterine activity are graphically demonstrated by the external tocograph. The pattern of normal uterine motility in pregnancy, labour and the puerperium is one of recurring waves of contraction (Fig. 2). Each contraction increases in intensity to an acme, which is sustained for a short time, then declines, to be followed by an interval of relaxation; systole is usually moderately abrupt, diastole more gradual.

In normal labour, succeeding contractions are characteristically of equal intensity and duration and recur at regular intervals, so that each contraction wave and its following trough can be superimposed on its neighbour. Compared with the regular curves of the first stage of labour, the

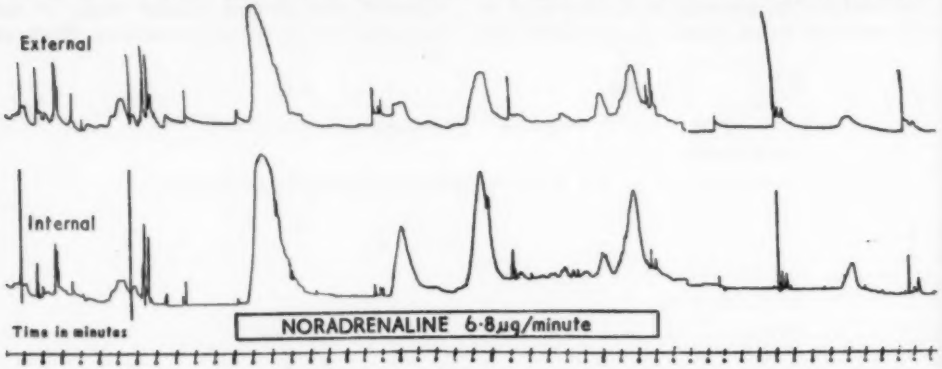

FIG. 3

Synchronous internal and external tocography. Puerperium 3rd day. Internal recording by intra-uterine balloon. The effect of Noradrenaline 6·8 µg./minute, i.v.

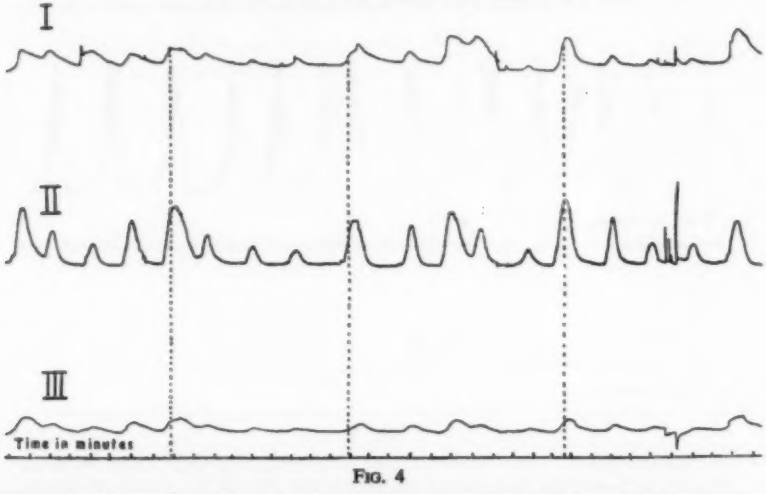

FIG. 4

Three-channel recording. Labour 1st stage. I: Upper zone. II: Middle zone. III: Lower zone.

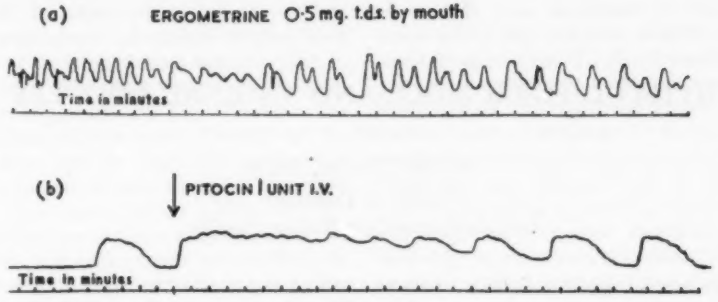

FIG. 5

The effect of drugs on uterine activity. (a) Ergometrine 0·5 mg. by mouth t.d.s. for 3 days. Puerperium 6th day. (b) Pitocin I u., i.v. Puerperium 3rd day.

contraction waves of the second stage are crowned by up strokes caused by the contraction of the "secondary powers".

The tocograph is uninfluenced by normal respiratory movements, but sudden violent contractions of the abdominal muscles, such as are produced by coughing or vomiting are recorded, while foetal movements too may be demonstrated (Fig. 2). The patient can be allowed a wide range of movement for the tocograph records equally well whether she is lying on her back or on her side. Movement from one position to the other may cause an alteration in the base line or "tone" but this can be readily corrected.

The quality of the records to be obtained by the external tocograph can be judged by comparing combined synchronous internal and external recordings. Figure 3 illustrates the close correlation between the two records which is usually evident.

The 3-channel recording illustrated in Figure 4 shows the coordination of uterine action in upper, mid and lower uterine zones, which characterizes normal labour.

Figures 3 and 5 demonstrate the influence of certain drugs on uterine activity. These and the other tracings are produced merely to indicate the utility and scope of the method of external tocography described; it is hoped to give a more detailed description of uterine activity and its response to drugs in a later communication.

SUMMARY

(1) A new multichannel external tocograph is described and a preliminary account of its use in operation presented.

(2) Characteristic features of uterine activity as demonstrated by the tocograph are graphically recorded.

The instrument described in this paper was constructed for me by Mr. T. Wright, Oxford. I am greatly indebted to him not only for his skill and care but in addition for much technical advice.

I also wish to thank Professor J. Chassar Moir for permission to publish this work and for his encouragement at all times.

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HYDATIDIFORM MOLE AND VAGINAL NODULES

BY

MAGNUS HAINES, M.D.

Director of Pathology

Chelsea Hospital for Women, London

THE appearance of a vaginal nodule in a patient with a degenerative or malignant lesion of the chorion is an event of sudden onset which is often taken to indicate an unfavourable prognosis.

The following case history describes a patient who was treated surgically 5 years ago for a hydatidiform mole diagnosed after a vaginal nodule had been discovered.

CASE REPORT

Case 1. Mrs. I.W., aged 45 years had had 2 children and 0 miscarriages. The last menstrual period was on 30th April, 1949. Before this periods had been regular. There was some vaginal spotting for 2 or 3 days starting on the 28th May. On 30th June there was heavy vaginal bleeding which lasted for 2 days. Intermittent bleeding occurred from mid-July. Abortion was presumed to be inevitable. Dilatation and curettage was planned but a vaginal cyst was found on the 26th July. Part of the cyst was removed for biopsy on the 15th August. During this time there was a steady increase in the size of the abdomen. Vomiting had been severe in the early part of the pregnancy. This did not occur during the 2 previous pregnancies. The chest X-ray was normal. Histological examination of the biopsy showed the nodule to be composed of haemorrhage associated with trophoblastic cells. In fact the pathologist Dr. G. L. Timms stated that the appearances were comparable to those of syncytial endometritis.

The patient came to England under the care of Mr. Charles Read who advised hysterectomy. The nodule at this time, 14th September, had healed. The uterus was the size of a 24-weeks pregnancy. The blood pressure was 190/110. There was a brownish discharge from the cervical canal. The external os admitted one finger and there was a small polyp protruding from it.

A total abdominal hysterectomy with the removal of both tubes and ovaries was done on the 26th September. Convalescence was uneventful. The patient returned to Kenya and she was alive and well 5 years later.

Biological tests for pregnancy were carried out pre-operatively using both the male toad (*Bufo bufo*) and the Friedman tests. The following results were obtained: the male toad test was positive in a dilution of 1 : 250 and the Friedman test was positive at 1 : 1000. Qualitative pregnancy tests were positive until the 9th post-operative day and they remained negative up to the time of the last test which was made on the 57th post-operative day. These findings were of a confirmatory nature only. They did not have any diagnostic significance except in so far as they indicated that no areas of functioning trophoblast in the lungs or elsewhere remained after the hysterectomy.

THE OPERATION SPECIMEN

The uterus and adnexa (Fig. 1) were available for examination. The soft regularly enlarged uterus measured 21 by 16 by 9 cm. On bisection the wall of the uterus was thinned out, measuring 0·5 to 1·0 cm. in thickness. The dilated cavity was filled with grape-like chorionic villi typical of vesicular mole. No embryo or sac was found Distended vesicles had permeated the uterine wall in a few places (Fig. 1) but these areas were not associated with haemorrhage. The cervix showed normal pregnancy changes. The ovaries were not enlarged. The right on bisection showed follicle cysts only. The left showed a firm round nodule 1 cm. diameter which on bisection (Fig. 2) was found to be a small cyst with a thick yellow wall.

Histological examination. Sections were made from several blocks of myometrium to include vesicles, and from the left ovary. Sections of the vaginal biopsy were also studied by kind permission of Dr. Timms. The mole was composed of numerous chorionic villi of variable size. Occasional vesicular villi were seen in the blood vessels of the myometrium (Fig. 4). Each villus showed copious gelatinous avascular stroma covered by trophoblast in two recognizable components or layers (Fig. 5). It is noted that, though these trophoblast covered villi were present within the myometrium, they were associated with neither haemorrhage nor muscle

cell necrosis. In other areas seen in sections from the placental site the normal trophoblastic penetration of the myometrium was seen (Fig. 6) associated with only slight muscle cell necrosis and chronic inflammation. The specimen was classified as an invasive mole. Though the invasiveness can only be regarded as slight it affected a large area of uterine wall. The nodule in the left ovary was a corpus luteum of pregnancy somewhat smaller than might be expected. It had an internal collagenous membrane 1 to 2 mm. thick lined by endothelium (Fig. 3). The membrane enclosed a cystic cavity 5 to 7 mm. in diameter. The outer rim of the corpus luteum was from 2 to 3 mm. thick. The periphery showed a reduced amount of festooning. Though theca cells elsewhere in the ovary showed luteinization they did not show this change except to a minor degree in and around the corpus luteum. These appearances may be interpreted as showing regression in a corpus luteum of pregnancy. The right ovary showed two small theca-lutein cysts. The vaginal biopsy showed fresh and old blood in connective tissue beneath normal vaginal epithelium (Fig. 7). Syncytial cells were scattered in the oedematous connective tissue and were seen associated with blood spaces. The biopsy appearances had all the characteristics of a benign trophoblastic nodule following a haemic embolus to this site.

Nature of Vaginal Nodule

It has been mentioned already that the histological picture of the vaginal nodule in the case reported was comparable to that of syncytial endometritis. This condition as seen in curettings and in hysterectomy specimens is characterized by a persisting and even accentuated permeation of the endometrium and adjacent myometrium by detached or wandering trophoblast cells of the syncytial type—associated with more or less of an inflammatory reaction. These appearances in the uterus (Fig. 6) though sometimes mistakenly diagnosed as malignant are invariably associated with a good prognosis. To form the vaginal nodule in my case trophoblast cells have escaped from the uterine veins and lodged in the vaginal wall. These cells retaining their physiological property of erosion have wandered in the connective tissue where they are seen usually singly. As a result gross erosion of a blood vessel takes place quite frequently and, as in this case, haemorrhage occurs into the tissue which explains the sudden onset of a nodule. If biopsy be delayed trophoblast cells may not be found. The haemorrhage may have been so large as to prevent the cells from gaining or keeping a place of attachment necessary for their metabolic needs and thus they have not survived. Some nodules must be present often without being discovered and while some have been known to disappear spontaneously many others must do so unobserved. These vaginal nodules containing only trophoblast of the syncytial type are considered to be at most an aberrant physiological phenomenon and morphologically they do not indicate a malignant change in the chorion or mole. Their formation and regression is discussed in detail by Park and Lees (1950) in a general and very complete review of chorion carcinoma.

The Significance of the Vaginal Nodule

Embolic phenomena such as the one described are characteristic of chorion carcinoma (chorion epithelioma, Mathieu, 1939) but, ever since the time of Schmorl's papers in 1904 and 1905, it has been held that in normal pregnancy trophoblast with or without chorionic villi can be disseminated (deported) via the haemic route to the lungs, vagina, vulva, etc.

In consultation with Dr. K. J. Randall I have recently studied biopsy material from a vaginal nodule in a patient (Case 2) who subsequently had a normal delivery with a normal placenta (Caturani and Gunn, 1955). At the 20th week of pregnancy the patient, aged 26 years, was found to have a bluish nodule beside the urethra. The histological appearances (Fig. 8) were almost identical with those in Case 1. Our acquaintance with such findings and their significance in cases of syncytial endometritis allowed us to make a correct diagnosis of this paraurethral nodule in a normal pregnancy which had a successful outcome without complications.

Mr. J. R. Dickinson has supplied me with

notes of another patient, Case 3. During evacuation of a hydatidiform mole a nodule was seen in the vagina. On biopsy the histological appearances were similar to those in Case 1 but at the time were otherwise interpreted (Fig. 9). The patient refused any further treatment. She returned to hospital 13 months later and was delivered of a normal male infant. No abnormality was found on vaginal examination postpartum. The benign nature of this vaginal nodule is indicated by its spontaneous resolution after biopsy.

It is interesting to note that Brews (1939) found no example of a vaginal nodule in 100 cases of hydatidiform mole though there was 1 case of secondary chorion carcinoma in which vaginal nodules disappeared after hysterectomy. This patient was alive and well 10 years later (Brews, 1950). There was only 1 case of vaginal nodule in a group of 41 patients with hydatidiform mole described by Hunt *et al.* (1953). However Laqueur (1945) described a case (his Case 7) almost exactly the same as my Case 1. In addition to trophoblast cells he found some villi covered with trophoblast and others showing only the outline of villi. In support he has cited cases by Gygax (1931) and by Wegelin (1936) in which a vulval nodule was associated with a hydatidiform mole.

Malignant disease, i.e., chorion carcinoma is usually diagnosed, or at least suspected in the presence of a vaginal nodule, as in the cases described and Willis (1952) mentions that the discovery of nodules may constitute the first indication of the disease. As a matter of fact vaginal nodules were present in 16 per cent of 74 cases of chorion carcinoma reported by Novak (1954) which is lower than the general figure of 50 per cent given by Hertig (1950). Although a suspected diagnosis of chorion carcinoma may not be discarded lightly, there is evidence to show that in some instances the appearance of a vaginal nodule has not such an unfavourable significance. Nodules of trophoblast may occur in normal pregnancy and I have given one example in Case 2. Some may pass unobserved. Such nodules occur and are found more frequently in association with benign and invasive hydatidiform moles than in normal pregnancy, but as shown by my Cases 1 and 3 they do not indicate that the mole is malignant —in the sense that it has become a chorion carcinoma.

The clinical or naked eye appearance of these nodules would appear to be similar in the 3 instances of pregnancy, hydatidiform mole and chorion carcinoma. On inspection, the nodule—there may be more than one (Brews, 1939; MacRae, 1951)—is raised above the mucous membrane, measures up to a few centimetres in diameter, is red or purplish in colour and bleeds easily on palpation. Bleeding from the nodule may be considerable and may cause serious difficulty especially after radiotherapy. These appearances will be modified if there is ulceration of the mucous membrane covering the nodule.

Certain distinguishing features may be found in the histological examination. It has been stated above that where the haemorrhage in the nodule is excessive no trace of trophoblast or even of ghost villi may be found. The presence of chorionic villi in the nodule is generally accepted as evidence against though not entirely excluding chorion carcinoma (Novak, 1954).

No villi were found in the biopsies (Cases 1, 2 and 3) described by me. There are two distinct and characteristic types of histological pattern to be seen in the vaginal nodules. Though intermediate patterns may occur I have not yet seen them. The first pattern is the result of an embolus from a chorion carcinoma and it is well illustrated and described by MacRae (1951). His vaginal biopsy and post-mortem sections showed "clumps of polyhedral Langhans' cells with hyperchromatic nuclei; and there were runs of syncytium with nuclei irregularly interspersed in the cytoplasm, which was excessively vacuolated. Blood vessels were seen to be blocked with tumour emboli and there was much haemorrhage." Such findings in a biopsy of the vagina in the presence of a lesion of the uterus must surely demand hysterectomy with the expected diagnosis of chorion carcinoma.

The alternative histological pattern is that described with the 3 cases reported in this paper. Here trophoblast cells which are of the syncytial type are found dispersed in the connective tissue and are seen in association with the vascular endothelium. The nuclei are often large, usually pyknotic. Mitotic figures are not characteristic

FIG. 1

Case 1. The whole uterus bisected coronally. Villi in myometrium marked by arrow. (Half natural size.)

FIG. 2
Left ovary, thick walled cyst. (Natural size.)

FIG. 3
Histology of left ovary. Corpus luteum of pregnancy with inner hyaline membrane. H. & E. ×7.

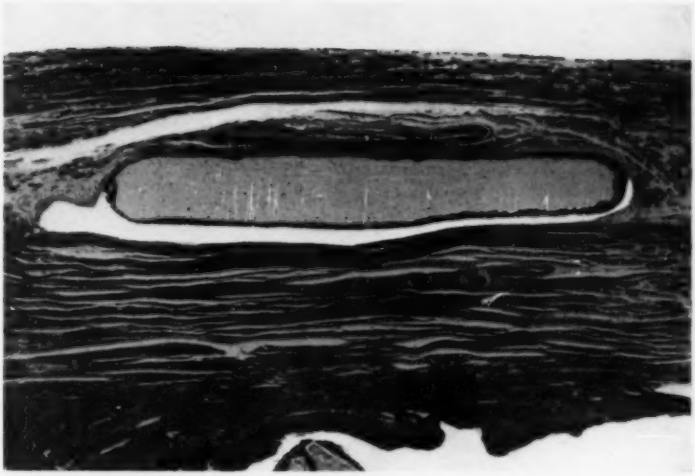

FIG. 4

Case 1. Wall of uterus showing chorionic villus within a vein. H. & E. ×9.

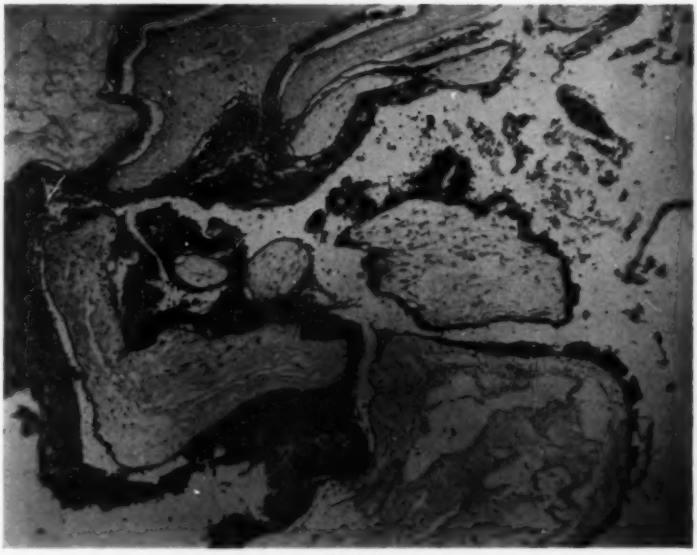

FIG. 5

Case 1. Large vesicular chorionic villi with two layers of trophoblast. H. & E. ×40.

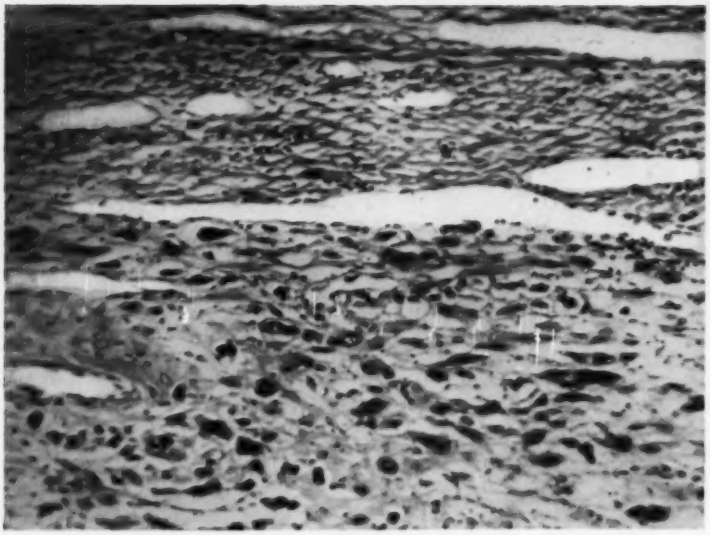

FIG. 6

Case 1. Placental site—trophoblastic (syncytial) permeation of myometrium. H. & E. ×75.

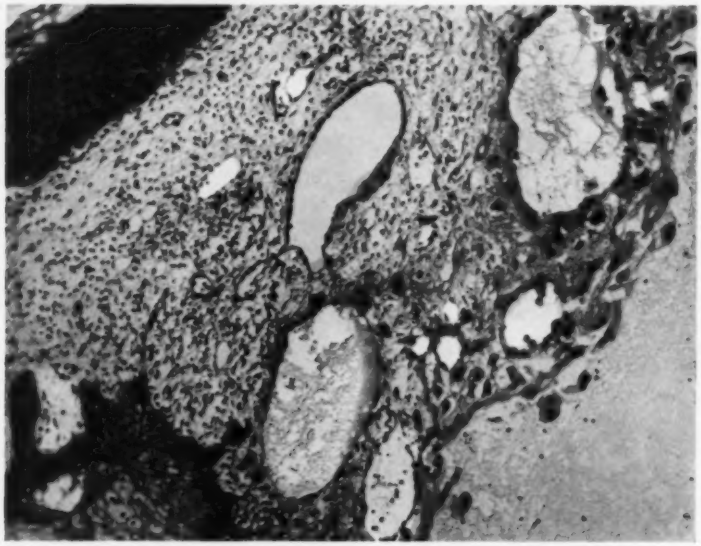

FIG. 7

Case 1. Vaginal biopsy. Scattered syncytial cells in connective tissue and associated with blood vessels. H. & E. ×75.

M.H.

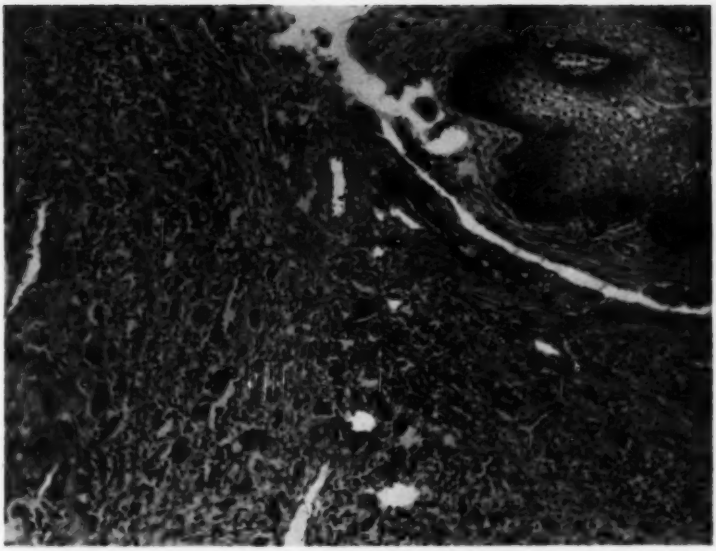

FIG. 8

Case 2. Vaginal (paraurethral) nodule in normal pregnancy. Scattered syncytial cells in the connective tissue. H. & E. ×100.

FIG. 9

Case 3. Vaginal nodule from hydatidiform mole—spontaneous cure. H. & E. ×40.

M.H.

nor are they usually seen in chorion carcinoma (Novak, 1954). These cells are in fact wandering trophoblast cells which, as mentioned before, are frequently seen in the myometrium in the region of the implantation site often well away from the ovum. Cytotrophoblast (Langhans' cells) is not seen in these benign nodules. When present in a vaginal biopsy syncytial cells are often misinterpreted, chiefly, one supposes, because they often have deeply stained nuclei.

The same holds for the uterine lesion which is frequently mistakenly diagnosed as malignant though such cases are invariably associated with a good prognosis as shown by Hertig (1947) in his description of 7 cases of syncytial endometritis. The probability is that vaginal nodules of the second type described are all associated with physiological or benign lesions and do not call for radical treatment. On the other hand it is conceivable, though I think unlikely, that malignant lesions might give rise to an embolus of this benign histological type.

In an account of the Mathieu Memorial Chorionepithelioma Registry, Novak (1954) lists 85 cases which were wrongly diagnosed as chorion carcinoma and doubtless many of them received treatment for malignant disease. It is suggested that hysterectomy, unless indicated for other reasons, is not usually justifiable on the basis of a vaginal nodule of the second type described. These nodules may be labelled metastatic, thus connoting a malignant state. Park and Lees (1950), in their account of regression of vaginal metastases, are not offering good advice when they state that such vaginal nodules must be "metastatic by any definition of the term". They agree that the nodule is formed by haemorrhage in association with trophoblast which has been deported by the haemic route to the vaginal wall—an embolus in fact. Unless there is evidence that embolic cells grow and proliferate in their new situation there is no justification for describing these nodules as metastases (Willis, 1953). It will be remembered that the growth in the size of the nodule which is often rapid is due to haemorrhage and not due to cell proliferation.

Nodules with this structure are to be considered simply as resulting from embolism and are not true metastases. Far from being pathognomonic of chorion carcinoma they suggest the presence of a benign molar pregnancy and have occurred in normal pregnancy. Such nodes described as carcinomatous as in my Case 3 have disappeared spontaneously. It would be interesting to reassess the pathological material from cases classified as "chorion carcinoma with metastases" in the light of what has been said about the structure and behaviour of trophoblastic nodes in the vagina. This aspect is fully reviewed by Park and Lees (1950).

Biological pregnancy tests, though helpful, have at best only a probability value in the management of cases of hydatidiform mole and chorion carcinoma (Hertig, 1950). It is certain that these tests cannot be used to distinguish between the two lesions. The same conclusions may be applied to the use of the test in cases of vaginal trophoblastic nodule. Positive results may be expected for some weeks at least after the evacuation of the uterus or the passage of a hydatidiform mole but a trophoblastic node *per se* of the type described is not necessarily associated with a positive test because the reacting gonadotrophins are believed to be a function of the cytotrophoblast and not of the syncytium (Haines *et al.*, 1954).

Vaginal Nodules Occurring During Pregnancy

During pregnancy the discovery of a vaginal nodule of the type described is uncommon. As stated, the incidence of vaginal metastases in chorion carcinoma varies from 16 to 50 per cent. That nodules occur also in hydatidiform mole and even in normal pregnancy is not perhaps so well known and it is probable that many cases of benign mole have been classified as chorion carcinoma solely for the reason that a vaginal nodule was present.

MacRae (1951) has described the exceptional case where a normal infant was delivered from a patient with chorion carcinoma and vaginal deposits. He has pointed out that Walthard (1907) and Fikentscher (1941) had previously described cases of chorion carcinoma which showed vaginal nodules during pregnancy. Mathieu (1939) mentioned one case of chorion carcinoma coincidental with pregnancy and

Hertig (1950) has drawn attention to the fact that the diagnosis of chorion epithelioma at the time of the initiating pregnancy is probably impossible except in the excessively rare instance of coincidental metastases.

It has been stated already that a vaginal lump seen during pregnancy may arise from a benign or relatively benign lesion and it is important before starting treatment to determine its nature as far as possible. This can be done in most cases by histological examination. Furthermore, it has been shown that a nodule composed of syncytiotrophoblast can arise quite as suddenly, and look the same macroscopically, as the dreaded metastasis from a chorion carcinoma.

The syncytial nodule may be associated with a normal pregnancy (Case 2), but it is more likely to come from a hydatidiform mole, as in Cases 1 and 3. Awareness of this phenomenon of "physiological embolism" may prevent unnecessary interference with a normal pregnancy or too radical treatment of a benign mole.

Each case must be assessed separately and borderline cases will appear occasionally. The following brief details, as yet unpublished, are given by courtesy of Dr. Arthur Hertig (1954) and Dr. D. Brown, pathologist at Beverly Hospital, Massachusetts: Mrs. D.H., a 39 year old para-8, gravida-9, was admitted to hospital with a 6-weeks history of vaginal bleeding. Because of her obesity it was difficult to tell whether or not she was pregnant. On vaginal examination a nodule was found and biopsied. A uterus containing a hydatidiform mole was removed and the patient remained well for 1 year. Because of the malignant pattern seen in the biopsy the case has been recorded as a chorion carcinoma coincidental with a hydatidiform mole.

Although there is a difference in the biopsy findings in the two cases this case is similar to my Case 1, where the vaginal nodule was a benign trophoblastic node.

Summary

A case is described of a vaginal embolus from a uterine vesicular mole treated surgically with a 5-year follow-up.

The nature and significance of the trophoblastic nodule in this and 2 other cases are discussed.

The results of biological pregnancy tests have little influence on the differential diagnosis of such cases.

A brief review is given of the coincidental occurrence of vaginal nodules with normal pregnancy, hydatidiform mole and chorion carcinoma.

Acknowledgments

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The specimen (Fig. 1) was shown at a meeting of the Obstetric Section of the Royal Society of Medicine (Haines, 1950).

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THE EFFECT OF OVARIECTOMY ON THE DISTRIBUTION OF LIPOID IN THE GENITAL TRACT OF THE MATURE VIRGIN GUINEA-PIG

BY

R. S. SNELL, M.B., B.S., M.R.C.S.

AND

T. NICOL, M.D., D.Sc., F.R.C.S., F.R.S.E.

Department of Anatomy, King's College, University of London

NICOL and Snell (1954a) showed that during the oestrous cycle lipoid is present in the epithelium lining the uterine horns and distal part of the uterine body and is most intense during the period of activity of the corpus luteum. They also showed that lipoid is practically absent from the epithelium of the uterine horns about the time of implantation and that in the stratum compactum a small number of large lipoid-containing cells is present throughout the cycle, being greatest in number at about the 11th day. The presence of the lipoid was regarded as evidence of increased cellular metabolism. In contrast it was found that lipoid only occurs in the epithelium of the lower cervix and vagina at oestrus and the appearances are those of fatty degeneration.

The present research was designed to study the effect of ovariectomy on the above distribution of lipoid in the different parts of the genital tract of the mature virgin guinea-pig.

MATERIAL AND METHODS

Seventeen virgin guinea-pigs aged about one year were used in the investigation and all were known to have a regular oestrous cycle, as verified by the vaginal smear technique (Stockard and Papanicolaou, 1917; Selle, 1922). Each animal was double ovariectomized on the 9th day of the cycle. Groups of animals were then killed by chloroform at varying intervals after ovariectomy and the whole uterus and vagina were removed. All the specimens were fixed in 10 per cent formalin and frozen sections 10μ thick were made of the uterine horn, the upper and lower parts of the uterine body, the cervix and the vagina. The sections were stained with Sudan III for 15 minutes, then decolorized in 50 per cent alcohol and washed in distilled water. Haematin was used as a counter-stain. High concentrations of alcohol were avoided as these may dissolve some of the lipoid (Kaufmann and Lehmann, 1929; Romeis, 1929).

RESULTS

The amount and distribution of lipoid after ovariectomy is shown for the different parts of the uterus and vagina in Table I. The differences in the amount of lipoid that did exist between the animals of the same group would seem to be accounted for by the natural differences among animals (Nicol, 1933).

Uterine horns and proximal part of uterine body

At the ninth day of the cycle when double ovariectomy was performed a small or moderate amount of lipoid is present in the lining epithelium of the uterine horns and proximal part of the uterine body. There is also present in the stratum compactum a few large cells of rounded or irregular shape which contain coarse globules of lipoid in their cytoplasm. These cells are unevenly distributed around the uterine lumen and there is no obvious concentration either at the mesometric or antimesometric side (Nicol and Snell, 1954a).

After ovariectomy the lipoid in the lining epithelium disappears in 3 days and remains absent at 7, 10, 14, 21 and 28 days thereafter.

TABLE I

Showing Amount and Distribution of Lipoid in the Uterus and Vagina in 17 Mature Virgin Guinea-pigs Following Ovariectomy Performed on the 9th Day of the Oestrous Cycle

Time after ovariectomy when killed	No. of animal	Uterine horn and proximal part of uterine body		Distal part of uterine body	Lower end of cervix and vagina
		Amount of lipoid in lining epithelium	Number of large lipoid-containing cells in stratum compactum	Amount of lipoid in lining epithelium	Amount of lipoid in lining epithelium
3 days	148	−	++	+	−
	157	−	++	++	−
	154	−	++	+++	−
7 days	137	−	++++	++++	−
	134	−	++	+	−
	133	−	+	++	−
10 days	159	−	+	−	−
	150	−	−	−	−
	163	−	++	−	−
14 days	135	−	++	−	−
	141	−	++	−	−
	142	−	++	−	−
21 days	100	−	+	−	−
	138	−	+	−	−
	140	−	++	−	−
28 days	101	−	+++	−	−
	122	−	+++	−	−

− = Absent. + = Very small amount. ++ = Small amount.
+++ = Moderate amount. ++++ = Great amount.

The epithelial cells become slightly diminished in height but no other changes are seen in the lining epithelium. In contrast, the large lipoid-containing cells in the stratum compactum (Figs. 1, 2 and 3) gradually increase in number up to the 7th day after which the number fluctuates, being highest at 14 and 28 days and lowest at 10 and 21 days after operation. These results are shown graphically in Fig. 4.

Distal part of uterine body

At the ninth day of the cycle a great amount of lipoid is present in the lining epithelium of the distal part of the uterine body. The lipoid globules are coarse and are mostly concentrated in the infranuclear zone of the cells (Nicol and Snell, 1954a).

After ovariectomy the amount of lipoid in the epithelium gradually falls during the first 7 days,

the globules remaining concentrated below the nucleus (Fig. 5). From the 10th to the 28th day lipoid is found to be absent. The epithelial cells, as in the uterine horns, become slightly diminished in height.

Cervix and vagina

After ovariectomy the upper part of the cervix shows appearances similar to those seen in the distal part of the uterine body. In the lower part of the cervix and in the vagina the lining epithelium becomes thinned and the surface cells are nucleated; lipoid is, however, absent.

Discussion

Nicol (1935) described the lipoid appearances in the uterine horns of the double ovariectomized guinea-pig 4 weeks after operation. He found that lipoid was absent from the cells of the lining epithelium but the connective tissue of the stratum compactum contained a small number of lipoid masses.

Gilbert (1942) reported on the distribution of fat in the endometrium of the castrated rabbit. She found that 8 days after ovariectomy fat was present in small amounts in the cells of the lining epithelium both above and below the nucleus and that coarse fat globules were present in the stroma, even extending into the circular and longitudinal muscle. Twelve days after ovariectomy a very small amount of fat was present in the supranuclear zone of the cells of the lining epithelium and moderate amounts were seen in the stroma.

Alden (1947) working on the rat showed that during the first week after ovariectomy the uterine epithelium contained a considerable amount of lipoid. At the end of the second week the amount of lipoid became slightly reduced and at 30 days some regions were devoid of lipoid while others contained small amounts limited chiefly to the supranuclear zone of the cells.

In the guinea-pig it is known that during the oestrous cycle there is a cyclic appearance of lipoid in the lining epithelium of the uterine horns and distal part of the uterine body and that this coincides with the period of activity of the corpus luteum (Nicol and Snell, 1954a). The appearances suggested that the lipoid is an index of cell metabolism.

Nicol (1935) reported that lipoid can be produced experimentally in ovariectomized guinea-pigs by the injection of corpus luteum hormone preceded by small sensitizing doses of oestrogen, but not by corpus luteum hormone alone. It seems reasonable to conclude that the disappearance of lipoid after ovariectomy reported in the present researches is therefore due to the removal of the influence of the ovarian hormones.

The persistence of lipoid in the epithelium of

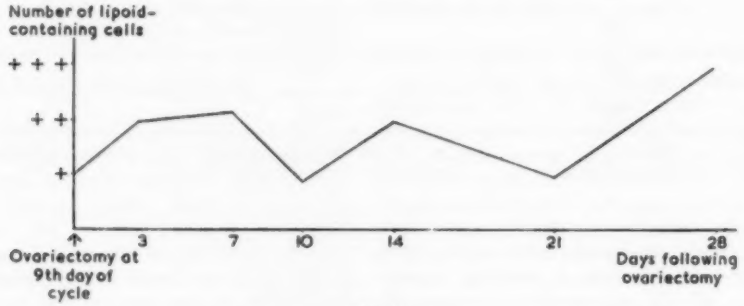

Fig. 4

Graph showing number of large lipoid-containing cells in stratum compactum of uterine horn and proximal part of uterine body in 17 mature virgin guinea-pigs following ovariectomy. The lipoid-containing cells increase in number up to the 7th day following ovariectomy after which the number fluctuates being highest at 14 and 28 days and lowest at 10 and 21 days after operation.

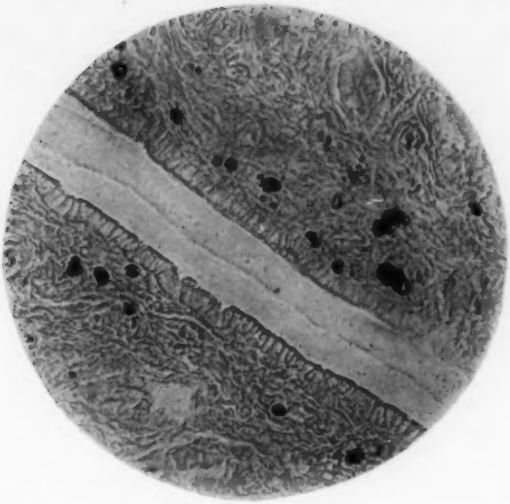

FIG. 1

Photomicrograph of section of uterine horn from mature virgin guinea-pig 28 days after double ovariectomy performed on 9th day of cycle. Shows lipoid-containing reticulo-endothelial cells in the stratum compactum. The lipoid globules appear black in the photomicrograph. Stained Sudan III. ×200.

FIG. 2

Higher magnification of section shown in Fig. 1. The lipoid-containing reticulo-endothelial cells in the stratum compactum are seen to be rounded or irregular in shape. The lipoid globules are of varying size and appear black in the photomicrograph. Stained Sudan III. ×600.

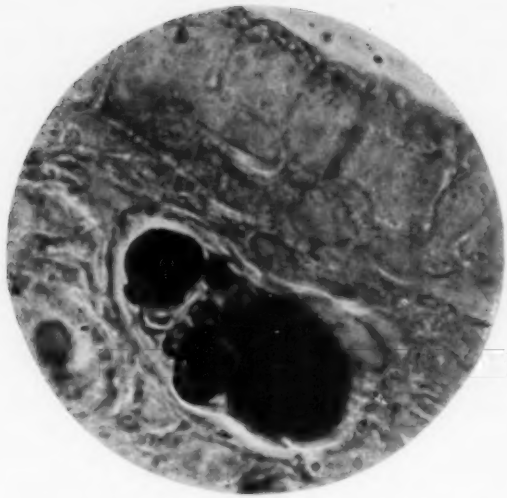

FIG. 3

Photomicrograph of one large lipoid-containing reticulo-endothelial cell in the stratum compactum from same section as Fig. 1. Shows cytoplasm packed with coarse and fine lipoid globules which overlap. The lipoid appears black in the photomicrograph. Stained Sudan III. ×1,400.

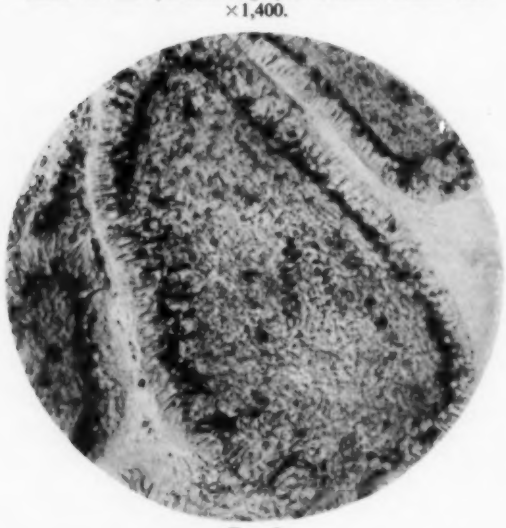

FIG. 5

Photomicrograph of section of distal part of uterine body from mature virgin guinea-pig 7 days after double ovariectomy performed on 9th day of cycle. The epithelium covering the villous-like processes contains a moderate number of lipoid globules concentrated chiefly in the infranuclear zone of the cells. The lipoid appears black in the photomicrograph. Stained Sudan III. ×200.

R.S.S., T.N.

the distal part of the uterine body for 7 days longer than in the uterine horns and proximal part of the uterine body suggests that the upper and lower ends of the uterus react differently to the ovarian hormones. This is to be expected in the guinea-pig for the two ends of the uterus differ in structure and function. The uterine horns and the proximal part of the uterine body have a thick smooth endometrium which possesses a large number of glands, whereas the endometrium of the distal part is thin and is thrown into complicated villous-like processes and the glands are few in number. Moreover, implantation in the guinea-pig occurs only in the uterine horns whereas the distal part of the body forms part of the birth canal.

The absence of lipoid from the epithelium of the lower cervix and vagina after ovariectomy at the 9th day of the cycle is also to be expected since lipoid is normally only present in the vaginal epithelium at oestrus when the epithelium is shed by a process of fatty degeneration under the control of oestrogen (Nicol and Snell, 1954b).

The large lipoid-containing cells in the stratum compactum of the uterine horns and proximal part of the uterine body fluctuate in number after ovariectomy, being most numerous at 7, 14, and 28 days after operation and least numerous at 10 and 21 days (Fig. 4). Nicol (1935) reported the presence of vitally stained reticulo-endothelial cells in the stratum compactum of the uterine horns in the guinea-pig and stated that some of these cells also contained lipoid globules in their cytoplasm. These cells are identical in size and shape to those described in the present research which are therefore believed also to belong to the reticulo-endothelial system. Furthermore, the results of the present investigation are in accord with the findings of Abou-Zikry and Nicol (1952) who showed that in ovariectomized animals there is a cyclic distribution of vitally stained reticulo-endothelial cells in the endometrium of the uterine horns independent of the ovaries, the cells being present in greatest number at what would have been the middle of the oestrous cycle had the ovaries been present. It is therefore suggested that the large lipoid-containing reticulo-endothelial cells in the stratum compactum of the uterine horns and proximal part of the uterine body also undergo a cyclic fluctuation in number independent of the ovaries and are possibly under the control of the pituitary, since the pituitary is known to possess an inherent cyclic activity (Smith and Engle, 1929; Wolfe, 1931; Wolfe, Cleveland and Campbell, 1932; Cleveland and Wolfe, 1933).

Gillman (1941) described the distribution of fat in the human endometrium and attempted to explain the presence of lipoid in the stromal cells. He believed that some of the lipoid was derived from degenerating red cells present in the endometrium at the time of menstruation but that all the fat did not emanate from this source since the amount in the stromal cells was not in proportion to the amount of extravasated blood or to the extent of damaged tissue present.

In the guinea-pig the lining epithelium of the uterus is shed at the third stage of oestrus and at this time haematomata may be seen in the stroma. Regeneration of the endometrium occurs at the fourth stage of oestrus and is complete in about 8 hours (Stockard and Papanicolaou, 1917). It would seem unlikely that the reticulo-endothelial cells in the stratum compactum play a major part in this process since in the intact animal only a few are present at oestrus. We believe therefore that the lipoid seen in the cytoplasm of the reticulo-endothelial cells is intimately related to the internal metabolism of the cells and has not been phagocytosed.

Summary

(1) The effect of double ovariectomy on the distribution of lipoid in the genital tract is recorded for 17 mature virgin guinea-pigs.

(2) In the uterine horns and proximal part of the uterine body lipoid was found to disappear from the lining epithelium 3 days after ovariectomy and remained absent at 7, 10, 14, 21 and 28 days thereafter.

On the other hand, large reticulo-endothelial cells containing lipoid were seen in the stratum compactum and appeared to undergo a cyclic fluctuation in number independent of the ovaries.

(3) In the distal part of the uterine body the amount of lipoid in the lining epithelium falls

gradually during the first 7 days after ovariectomy and from the 10th to the 28th day was found to be absent.

(4) The upper part of the cervix showed appearances similar to those seen in the distal part of the uterine body. In the lower part of the cervix and in the vagina lipoid was absent.

(5) The disappearance of lipoid from the lining epithelium of the uterus was shown to be due to removal of the influence of the ovarian hormones.

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AN ASSESSMENT OF THE VALUE OF ANTENATAL RADIOLOGICAL PELVIMETRY BASED ON 500 SUCCESSIVE PELVIMETRIC EXAMINATIONS

BY

G. W. PIMBLETT, M.A., M.B., D.M.R.

Consultant Radiologist

AND

T. G. E. WHITE, M.D., M.R.C.O.G.

Senior Registrar in Obstetrics and Gynaecology

Mayday Hospital, Croydon

INTRODUCTION

ANTENATAL radiological pelvimetry and cephalometry can provide accurate information on the cephalo-pelvic relationship which exists or is likely to exist at or near term. As disproportion in its widest sense is the chief cause of difficult childbirth, it is by the study of the bony architecture of the maternal pelvis and the size and position of the foetal head that radiology can be of great help.

This paper is an assessment of the value in obstetric practice of radiological pelvimetry based on 500 consecutive cases examined radiologically during 2½ years in a large obstetric unit.

Antenatal care of the pregnant woman was introduced in this country half a century ago by Haig Ferguson and J. W. Ballantyne. One of the benefits which was expected to arise from antenatal care was a reduction in the stillbirth and neonatal death rate arising from disproportion. That this reduction had not occurred was shown by the Ministry of Health report published in 1922. This showed that a great number of stillbirths and neonatal deaths which had been attributed to syphilis were in fact due to cerebral injury.

Twelve years later Wrigley (1934) pointed out that the management of cases of supposed minor degrees of disproportion was very unsatisfactory. Using figures from London Hospitals, he showed that labour was induced 14 times as often in one hospital as in another. Figures from five large maternity hospitals showed an infant mortality rate of just under 10 per cent in cases in which labour had been induced. These poor results were due to a diagnosis of disproportion where it did not exist. To overcome the difficulty in the diagnosis of contracted pelvis various instruments for internal pelvimetry were invented. These gave disappointing results and dropped into disuse.

This failure of clinical methods to solve the problem of the diagnosis of disproportion gave a great impetus to the development of techniques for radiological pelvimetry and cephalometry.

RADIOLOGICAL TECHNIQUE

A critical review of the many various techniques of pelvimetry and cephalometry is not relevant to this paper. The method used in this series is described briefly with emphasis on those points where it differs slightly from the generally accepted projections. It should be noted that, while the bi-parietal diameter is measured in either the lateral erect or the supero-inferior view, a check can be made in the postero-anterior projection or, failing this, the sub-occipito bregmatic diameter can be measured and used for comparison. This triple check ensures that a gross error does not occur.

The following are the routine projections used:

1. *Postero-anterior with patient prone to include the whole of the outline of the uterus*

This view is primarily for the study of the foetus which, in the postero-anterior view, is brought nearer to the film with less distortion and greater clarity than in the more usual antero-posterior film. Very few patients object to this position if a pillow is placed under the breasts and care and gentleness is taken in positioning them.

In this view, at term, the foetal skull lies, in the vast majority of cases, between 2½ and 3½ inches from the table top. The fatness or thinness of the patient very rarely makes more than 1 inch difference in this measurement. This is an advantage as it provides a further check on the foetal skull measurements estimated from the other views.

2. *Supero-inferior view of pelvic inlet*

The angle of the back rest is set at 60 degrees. The patient leans comfortably back and is positioned over the cross marks on the table top. Overlapping of the posterior and inferior pubic rami so that the obturator foramen cannot be seen is generally an indication of correct positioning, but this is not invariably the case if there is asymmetry of the pelvis due to any cause. The posterior limit of the true conjugate is not always plain in this view, especially if there is a false sacral promontory. Reference to the film of the lateral projection with comparison of the true conjugate measurement estimated from it will, however, show what bony point should be taken in the supero-inferior view. As pointed out by Williams (1943) a slight error in the parallelism of the brim and the film does not lead to serious inaccuracy providing the centering is at, or near, the mid point of the true conjugate. The distance from the top of the symphysis pubis to the table top is measured in each case; it is nearly always between 3 and 5 inches.

3. *Lateral erect*

This is the most important single view (Fig. 1). As Williams (1943) pointed out, diameters measured some distance from the centering point cannot be completely corrected by simple arithmetic correction graphs representing different object-film distances. This particularly applies in the lateral view to the posterior sagittal diameter of the outlet and to the foetal head if it lies high up above the brim of the pelvis and therefore far from the centering point.

4. *Outlet view*

The classical positioning of Chassard and Lapiné (1923) was used. The slight forward angulation (10°) of the central beam advocated by Williams (1943) has been found to be of value. This projection generally presents little difficulty.

The position of the ischial spines is important in relation to the sub-pubic arch. Apparently there still appears to be some doubt as to whether the bi-parietal diameter of the foetal skull normally passes in front of or behind the ischial spines during its descent of the birth canal.

In those few cases in which films have been taken late in labour with the head low down in the cavity, the bi-parietal diameter has been seen to pass in front of the ischial spines but, where these are not symmetrically placed, it would seem possible in some cases for one parietal eminence to pass behind and one in front of the ischial spines. Obviously prominent ischial spines lying far forward, in combination with a narrow sub-pubic arch, are of more serious significance than those which lie well back towards the lower sacrum.

Cephalometry

It is only lately that the question of the growth of the foetal head during pregnancy has been satisfactorily cleared up. Previously there were many conflicting and irreconcilable statements. Scammon and Calkins (1929) stated that the size of the foetal head was constant in all foetuses at the same age, i.e., 97·4 mm. bi-parietal at birth, and this was supported by Reece (1935).

Macdonald (1952) affirmed that the foetal skull did grow in the last few weeks of pregnancy and explained why Josephs (1949) had been led to state otherwise. Lately Macdonald (1953) enlarged on his previous paper and Crichton (1952, 1953) has ably summarized the previous literature and from further observations supports

Macdonald's view. One comes back therefore to the commonsense conclusion that the size of the foetal head varies from case to case and that it continues to increase in size during the latter weeks of pregnancy.

Accurate cephalometry by radiological means is possible. This has been established beyond doubt. Admittedly there are many cases in which it is not easy.

The problems of cephalometry are not simply the technical problems of accurate measurements of a given diameter of the foetal skull. The difficulty is to decide which measurements should be taken, and how they should be used. Most methods use the bi-parietal diameter of the foetal skull on the grounds that this is the widest diameter in a well flexed head. From the recent work of Crichton (1953) it would appear that reliance cannot be placed on estimates based on measurement of one diameter. This has been confirmed by numerous cases in the present study.

The time at which cephalometry should be carried out is another problem which has assumed greater importance than it was given originally. The only way of ensuring accurate measurements is to have them taken as near the date of delivery as possible. Estimates based on measurements taken 3 or 4 weeks earlier will be unreliable in a considerable percentage of cases. When possible, all pelvimetry examinations were made at 38th/39th week of pregnancy, but if they were done earlier the epiphyseal development (such as lower end of femur at 36 weeks) was correlated with the size of the foetal head in checking the maturity and 0·1 centimetre to 0·12 centimetre added to the bi-parietal diameter for each week which had to elapse before the expected date of confinement.

The actual foetal skull measurements are first taken from the lateral view. A further film with higher centering may occasionally have to be taken if the head is very high and so subject to distortion in the conventional view.

The height of the foetal skull above the pelvic brim is measured and used to give the correction for its measurement in the inlet view.

A careful check on the accuracy of radiological estimation of the foetal skull measurements has been undertaken by measuring the foetal head after birth with engineers calipers (Fig. 2). In 88·9 per cent of cases so checked within 7 days, a difference of less than $\pm 0{\cdot}2$ cm. in the measurement of the bi-parietal diameter was recorded. This is almost within the experimental error of measuring the head after birth with calipers, as comparison of the readings of 3 independent people has shown (Table I).

In order to determine how much reliance could be placed on the caliper measurements which were to be used as a test of the accuracy of radiological cephalometry, two colleagues and one of the authors measured the bi-parietal diameter of the heads of 25 unselected babies which were in one of the nurseries. All the measurements were completed within one hour. The results were as follows:

TABLE I

	No. 1 cm.	No. 2 cm.	No. 3 cm.
1	9·8	9·8	9·8
2	9·6	9·6	9·5
3	9·1	9·2	9·2
4	9·6	9·6	9·6
5	9·6	9·7	9·8
6	9·5	9·5	9·6
7	9·9	9·9	9·8
8	9·0	9·1	9·0
9	9·7	9·7	9·6
10	10·0	9·8	9·8
11	9·4	9·5	9·5
12	9·6	9·6	9·6
13	9·7	9·6	9·6
14	9·3	9·2	9·3
15	9·4	9·4	9·3
16	9·1	9·0	10·0
17	9·5	9·5	9·5
18	9·5	9·4	9·4
19	9·0	9·1	9·1
20	9·3	9·3	9·2
21	9·6	9·6	9·6
22	9·6	9·6	9·5
23	9·3	9·1	9·1
24	9·5	9·5	9·4
25	9·0	9·0	8·9

The same caliper and calibrated scale were used by all three observers. As will be seen from the figures the same result was obtained by all three observers in only 5 cases. In 18 cases two of the observers got the same figure. In case No. 5 three different measurements were obtained, while in Case 16 there was a gross

DEMONSTRATION CHART

PELVIMETRY MEASUREMENTS

TRUE CONJUGATE 10·9 cm.

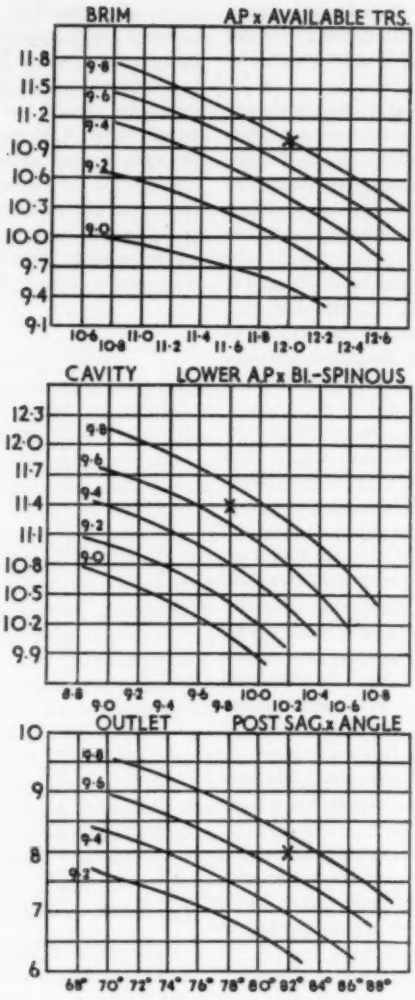
AVAILABLE TRANSVERSE 12 cm.

LOWER ANTERO-POSTERIOR 11·4 cm.

INTERSPINOUS 9·8 cm.

POSTERIOR SAGITTAL 8·0 cm.

SUBPUBIC ANGLE 82°



FOETAL MEASUREMENTS

BIPARIETAL FOETAL SKULL 9·6 cm.

MATURITY OF FOETUS 40 weeks

REPORT:
Gynaecoid brim.
Sacrum well hollowed.
Vertex presentation.
Left occipito anterior.
No disproportion shown.

GROUP A

FIG. 3

FIG. 1

Lateral Pelvimetry. The true conjugate, lower antero-posterior and posterior sagittal diameters are marked.

FIG. 2

A caliper as used for measuring the bi-parietal diameter of the foetal skull.

G.W.P., T.G.E.W.

FIG. 5

Clinical measurements of the diagonal conjugate on a dried pelvis. Note the piece of lead touching the sacral promontory.

FIG. 6

Clinical measurement of the diagonal conjugate in a patient with a contracted pelvis. Note the piece of lead has not reached the sacral promontory.

error by one observer when 10·0 cm. was recorded where 9 cm. was intended.

From this it will be seen that where the radiological measurement is within 2 mm. of that obtained by caliper this may be considered an accurate radiological measurement.

It was generally possible to measure the bi-parietal, the sub-occipito bregmatic and the occipito-frontal diameters by study of the lateral, the inlet view and the postero-anterior prone projection. Only the bi-parietal diameter was used in the forecast graph but a check was made of the occipito-frontal and sub-occipito bregmatic measurements to ensure as far as possible that a gross error had not occurred in estimating the bi-parietal diameter.

In this series it has been found, in agreement with Crichton (1953), that in some cases the rate of growth of the occipito-frontal and bi-parietal diameters is not the same, and that the measurements of the foetal skull do not bear a constant relationship to each other.

In this series the bi-parietal diameter of the mature foetus has varied from 8·7 cm. to 10·2 cm.

The Chassar Moir Chart

This method of reporting the results of radiological pelvimetry was described by Moir (1946, 1947, 1949).

The charts were built up by recording the outcome of labour in a large series of cases in which accurate data were available. The charts are not graphs and have no mathematical significance. Their great merit lies in the ease with which the salient features of a case can be seen by a glance at the chart. The radiologist writes a report in addition to the chart and places the case in one of three prognostic groups. A specimen chart is shown in Figure 3.

These charts have been favourably reported on by Kaltreider (1951, 1952) and Erskine, Kelham and Wium (1953).

The dividing lines (see chart) have been drawn up on a pure "trial and error" basis and it is open to obstetricians whose results do not conform with those forecast by the chart to collect a series of cases and plot a new series of charts to suit their own results. This is in fact being done by the authors who have found the cavity chart too pessimistic. Sufficient new points have been plotted to re-draw the 9·6 line (Fig. 4).

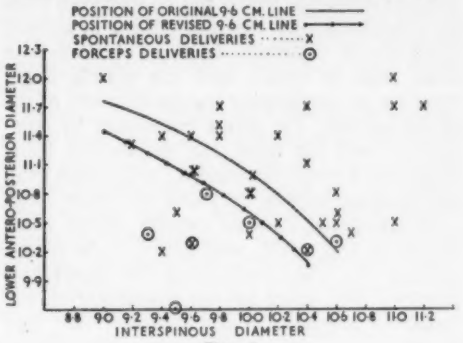


FIG. 4

Revised 9·6 centimetre line on Moir's cavity chart.

In the course of time sufficient cases may be available to enable the lines on the outlet chart, which also seems to be on the pessimistic side, to be replotted. In quite a number of cases the measurements, when plotted, fall outside the charts altogether. When the points fall above and to the right of the chart there is no difficulty as this means that the pelvis is above average dimensions. If the points fall outside the left hand margin certain difficulties arise as there must be some limit of the reduction of the transverse diameter of the pelvis beyond which a vaginal delivery is impossible. Erskine *et al.* (1953) found a similar latitude in the cavity and outlet charts and had the same doubts about the safety of projecting the bi-parietal lines to the left.

The clinical measurement of the diagonal conjugate

The majority of the cases in this series were selected for radiological examination by the method of head fitting. Cases selected for radiological examination as a result of the findings on vaginal examination were chiefly cases of suspected disproportion in the cavity or outlet. Despite the unequivocable findings of Howkins (1938) and Jacobs (1942) that accurate measurement of the diagonal conjugate by clinical methods is virtually impossible and that deduction of the true conjugate from the diagonal conjugate is so inaccurate as to be valueless for

obstetric purposes, these methods are still widely used. The difficulty of detecting contraction of the true conjugate would not be suspected from an examination of the illustrations in current textbooks of obstetrics. In these illustrations a huge hand is shown with the middle finger reaching or overlapping the promontory of the of the sacrum. The pelves are minute by comparison with the hand, the proportions being those which would be found if a large adult hand was photographed in the pelvis of a small child.

Inexperienced medical officers, when questioned on this point, were found to be of the opinion that they could reach the sacral promontory. The reason for this misconception was found to originate in the fact that they had practised measurement of the diagonal conjugate on a dried pelvis such as is used for instruction of students and midwives. The following experiment was carried out to demonstrate the difficulty of measuring the diagonal conjugate by clinical methods.

A small piece of lead was placed in the tip of the middle finger of a rubber glove. Wearing this glove, the fingers were inserted below the pubic symphysis of a dried pelvis which had a true conjugate of 11·6 centimetres. The sacral promontory was easily reached and a lateral X-ray photograph was taken (Fig. 5).

Using the same technique, the experiment was repeated during the puerperium in a patient with a true conjugate which was known to be 9·6 cm. Despite the laxity of the vagina and perineum and the short true conjugate, the sacral promontory could not be reached (Fig. 6). This experiment shows the impossibility of measuring the true conjugate by clinical means except in gross contraction of the brim.

The Clinical Material

The work on which this paper is based was carried out over a period of 2½ years ending in early 1953. The patients were all delivered in a maternity unit in which there are approximately 2,000 deliveries annually. This unit serves a population of 250,000 people. This paper relates to a consecutive series of 500 antenatal radiological pelvimetries carried out on patients referred in the latter weeks of pregnancy because of suspected disproportion.

In Table II an analysis of the figures from the authors' series, together with those from the series published by Williams and Arthure (1949), Erskine *et al.* (1953) and Weinberg and Scadron (1943) are given. These all show approximately 60 per cent of cases in the group without disproportion.

This is a measure of the value of unaided clinical judgment.

TABLE II

Prognostic Groups—Percentages

Prognostic Groups	A	B	C		
Authors' cases	65·4	26·2	8·4		
Prognostic Groups	**A**	**B**	**C**	**D**	**E**
Williams Combined Series	59·1	20·1	9·9	5·9	5
Prognostic Groups	**None**	**Minor**	**Disproportion Moderate**	**Severe**	
Erskine *et al.*	66·2	15·6	8·1	10·0	
Prognostic Groups	**A**	**B**	**C**	**D**	
Weinberg and Scadron	62	19	10	9	

Radiological pelvimetry was not confined to primigravid patients. A serious degree of cephalo-pelvic disproportion may be present in a woman who has had one or more spontaneous vaginal deliveries. The problem of why labour should be obstructed in one pregnancy and not in previous ones with babies of equal weight is difficult to solve. Only a small number of patients who had had a previous spontaneous delivery were radiographed, but where there had been a previous difficult forceps delivery or a Caesarean section radiological pelvimetry became almost a routine.

The approach described by Williams and Phillips (1946) has been taken as a guide in presenting the results and in assessing the correctness or otherwise of the radiological predictions.

In the present series cases have been divided into 3 groups, as suggested by Williams (1953).

These groups are as follows:

Group	*Relative Proportions*	*Likely mode of delivery*	*Qualifications*
A	No disproportion	Spontaneous	Easy low forceps
B	Definite disproportion	Difficult spontaneous or forceps delivery	Caesarean section for disproportion unlikely
C	Severe disproportion	Vaginal delivery even with forceps unlikely	Caesarean section probable

This was done after a considerable trial had been given to the use of five groups A—A/B—B—B/C—C corresponding to Williams's 5 groups shown below.

Group	*Relative Proportions*	*Likely mode of delivery*	*Qualifications*
A	No disproportion	Normal	Without reservations
B	No disproportion	Normal	With minor reservations
C	Minor disproportion	Difficult	Normal feasible
D	Moderate disproportion	Abnormal	Normal most improbable
E	Severe disproportion	Abnormal	Normal impossible

The use of three groups is more satisfactory for the following reasons: To attempt to forecast which patients will require a low forceps delivery due to a rigid perineum, or lack of maternal fortitude, requires consideration of the patient's mental and physical powers. This is a matter for clinical judgment by the obstetrician and cannot possibly be decided on the basis of radiological findings. It is thus unnecessary for the radiologist to divide the cases with no disproportion into those in which forceps will be required and those which will have a spontaneous delivery. To attempt to make this distinction is to attribute to radiological pelvimetry virtues which it does not possess and should not appear to claim to possess.

It is considered inadvisable to include a special group for cases with absolute disproportion in which elective Caesarean section is indicated as the method of delivery. The decision as to the method of delivery should be made by the obstetrician and not by the radiologist. The small percentage of cases in which the radiologist can say with certainty that elective Caesarean section is to be the method of delivery is illustrated by the figures from Williams and Arthure's series (1949). Out of a total of 300 cases only 9 were placed in group E, indicating absolute disproportion; of these 9 patients, 6 were given a trial of labour.

Erskine *et al.* (1953) used 4 prediction groups. These were based on the assumption that cases could be placed in the proper groups by the use of the measurements as shown on the chart. They defined their 4 groups in terms of millimetres of disproportion: e.g., "Minor disproportion. Disproportion of not more than 2 mm. on the brim chart or of not more than 4 mm. on the cavity or outlet chart."

They discovered that this was likely to lead to errors if allowance was not made for pelvic shape as well as size. "However, with increasing experience, certain modifications in the predictions have been made in the presence of such unfavourable factors as flattening of the sacrum, disproportion at more than one level, posterior position of the occiput, etc."

The Three Prognostic Groups

Group A as used in this series indicates the cases with no disproportion.

Group B as used in this series indicates that there is definite disproportion present, but not of such a degree that Caesarean section will be required. These cases are those in which a difficult vaginal delivery with or without forceps may be expected. Obviously those factors which are unpredictable by radiological examination may be responsible for a Caesarean section in some cases or a relatively easy labour in others.

Group C. This group includes all cases in which delivery by Caesarean section is probable.

The Assessment of the Accuracy of the Radiological Prediction of the Outcome of Labour

In assessing the accuracy of the prediction, most cases fell fairly easily into one of three groups—Correct, Incorrect or Not Assessable.

Group A. In Group A spontaneous deliveries

and easy low forceps deliveries were assessed as correct. Difficult forceps deliveries and Caesarean sections due to cephalo-pelvic disproportion were assessed as incorrect.

Group B. In Group B assessment was more difficult although the possibility of a correct forecast was, at first sight, greater. Group B contained the true borderline cases where there was definite cephalo-pelvic disproportion or some unfavourable factor in the pelvic architecture which would be expected to cause dystocia, but not of such a degree that Caesarean section would be necessary to effect delivery.

Where a Caesarean section was required after trial labour, which had been conducted under favourable circumstances, the forecast was considered as incorrect. Similarly, if an easy spontaneous delivery took place after a short labour the case would be placed in the incorrect group.

In some of these cases a spontaneous delivery was assessed as correct because it was clear that favourable, but radiologically unpredictable factors had combined to overcome the difficulties which existed. Forceps delivery was assessed as correct where it was clear that forceps had been used to overcome disproportion which was obstructing the progress of labour.

Group C. In Group C Caesarean sections after trial of labour and very difficult forceps deliveries have been assessed as correct. In one case a spontaneous delivery was considered correct in Group C, but generally spontaneous deliveries or easy forceps deliveries have been assessed as incorrect predictions.

Non-Assessable Cases. The term "non-assessable" has been used in the same way as by Williams and Phillips (1946). It contains those cases in which a proper test of the radiological prediction was not made. The majority of these cases were those delivered by Caesarean section without adequate trial of labour.

The non-assessable cases in the other groups are those in which, for reasons other than disproportion, there was operative interference, or in some cases the baby was delivered under such circumstances that a proper test of cephalo-pelvic relationships could not be made.

Incorrect Forecasts. In an analysis of the incorrect forecast cases no errors were detected in the actual pelvic measurements obtained by radiological pelvimetry but there is no satisfactory clinical method of making accurate internal measurements of the pelvis.

There was a considerable number of errors in cephalometry which did not lead to errors in prognosis, and are not included in the incorrect forecasts. Two main causes of these errors were discovered:

(1) In assuming that, where the bi-parietal diameter was not clearly seen, the measurement for the sub-occipito bregmatic diameter could be substituted for it. In some cases there is a significant difference between the length of these two diameters.

(2) In assuming that the rate of growth of the foetal head takes place at a constant and similar rate in all cases. When pictures were taken several weeks before the date of delivery and the bi-parietal diameter calculated by adding a certain amount for each week which had to elapse, errors arose when delivery took place before the expected date or when the rate of growth was different from that assumed. This error has now been eliminated by carrying out cephalometry at or after the 38th week of pregnancy where possible.

The cases in which the forecast has been considered to be incorrect have been due to failure to predict the effect on labour of abnormalities of the pelvic shape and size such as the relative importance of disproportion at certain levels or flattening of the sacrum.

The Group A Cases

Group A cases are those in which there is no disproportion and in which a spontaneous vaginal delivery is expected to take place. The majority of these cases are patients with a pelvis of normal shape and size. Where there is some reduction in the pelvic measurement accurate cephalometry is essential in order to determine whether there is disproportion or not. If the head is very large there may be disproportion even with pelvic measurements which are within the limits considered normal by some authors. It is thus not possible to say that all cases in which the pelvic measurements exceed a certain minimum should be in Group A or that, if measurements do not exceed a certain minimum,

the case must not be put into Group A. The group into which the case must be put must be decided after considering in each case the size and shape of the pelvis and the size of the foetal head.

Despite this refinement, which allowed some borderline cases to be placed in Group A by the use of Moir's charts, the majority of cases in Group A were cases in which, due to the ample pelvic measurements, cephalo-pelvic disproportion was unlikely to arise.

The percentage of cases in Group A in this series can be compared with the figures given in other published series. These figures are shown in Table III.

TABLE III

Williams and Arthure (1949) Combined Series	Weinberg and Scadron (1943)	Erskine (1953)	Authors
600 cases	280 cases	160 cases	500 cases
A plus B 79	A 62	1 66	A — 65
C 10	B 19	2 16	B — 26
D plus E 11	C 10	3 8	C — 9
	D 9	4 10	
Percentage figures			

From this it will be seen that the percentage of Group A cases in this series is lower than the comparable groups in either Williams's or Erskine's series and only a little above Weinberg and Scadron's figure.

Table IV shows an analysis of the cases in Group A.

All the 19 cases of Caesarean section were considered non-assessable. Of the 47 forceps deliveries, 3 were considered non-assessable and 1 an incorrect prediction. This leaves 43 forceps deliveries which were not due to disproportion between the head and the bony pelvis and therefore considered correct. There were 244 spontaneous deliveries as a vertex of which 2 were non-assessable and 17 vaginal breech deliveries all of which were assessable.

Incorrect Prediction. One case which occurred in the first 100 cases of the series was considered an incorrect prediction. The error arose in not paying sufficient attention to a flattened sacrum

TABLE IV

Group A, 327 Cases or 65·4 per cent of 500 Cases

	Total		Percentage of Total
Number of Cases	327		
Spontaneous Vertex	244		74·6
Vaginal Breech	17		5·2
Forceps	47		14·4
Caesarean section			
Vertex	16	19	5·9
Breech	3		
Not Assessable	22		6·7
Assessable	305		93·3
Correct	304		93·0
Incorrect	1		0·3
Correct as percentage of Assessable Cases		99·7	
Incorrect as percentage of Assessable Cases		0·3	

combined with an android brim in a pelvis in which the obstetrical conjugate was less than the true conjugate. The chart showed that there was just sufficient room for the head to pass. A persistent occiput posterior position combined with the other unfavourable factors led to a difficult forceps delivery. The case should have been in Group B.

THE GROUP B CASES

Group B cases are those in which there is some disproportion but in which a vaginal delivery with or without the help of forceps is to be expected. These are the true borderline cases whose management requires a high degree of obstetric skill if stillbirths are to be avoided on the one hand and unjustified Caesarean sections on the other.

There were 131 cases (or 26·2 per cent of 500 cases) placed in Group B. The details are shown in Table V.

The cases placed in Group B are sometimes nearly suitable for Group A and sometimes almost in Group C.

In assessing the accuracy of the predictions, cases in Group B which have had spontaneous vaginal delivery and all low and midcavity forceps deliveries have been assessed as correct. This means that only Caesarean sections or high forceps deliveries were considered to indicate

TABLE V

Group B, 131 Cases or 26·2 per cent of 500 Cases

	Total		Percentage of Total
Number of Cases	131		
Spontaneous Vertex ..	65		49·6
Vaginal Breech	3		2·3
Forceps	31		23·7
Caesarean section			
Vertex	31	32	24·4
Breech	1		
Not Assessable	27		20·6
Assessable	104		79·4
Correct	97		74·0
Incorrect	7		5·3
Correct as percentage of Assessable Cases ..		93·3	
Incorrect as percentage of Assessable Cases ..		6·7	

an incorrect forecast. Two cases delivered by Caesarean section were classified as non-assessable because the tests of labour were inadequate, 1 being only 6 hours with the membranes intact, and the other 17 hours in labour with no record of the state of the cervix or membranes. With the exception of these 2 cases there was some reason other than disproportion for the other 24 Caesarean sections which were considered non-assessable. One spontaneous delivery was non-assessable as the baby, which was stillborn, was premature. In the spontaneous delivery group the duration of labour was 17·7 hours. The forceps group had an average of 31·8 hours while the average for the Caesarean section group was almost double that of the spontaneous delivery group, being 33·7 hours.

Incorrect Predictions. In Group B there were 7 cases in which the radiological prediction was considered to be incorrect. The cause of the incorrect forecasts were as follows.

In 1 case there was an error in measuring the films. This led to a slightly more favourable prognosis than was justified, although the case would still have been in Group B with the corrected measurements. The remaining 6 cases should all have been in Group C.

In 1 case there was an error in cephalometry. In 2 cases the measurements were accurate but an unjustifiably optimistic prognosis was given. In the remaining 3 cases, insufficient weight was given to a combination of disproportion at the brim with disproportion at a lower level or a flattened sacrum or some other unfavourable feature.

As it is in Group B that trial labours ending in vaginal delivery, either spontaneous or assisted by forceps, should be found, it is appropriate to analyze the Group B cases according to the length of labour. The average figures given above are no indication of the length of labour in individual cases. The number of cases, expressed as a percentage of the total in each group, of forceps and of spontaneous deliveries, which were delivered in each 12-hour period, shows that there was a fairly high proportion of prolonged labours in both the forceps delivery group and in the spontaneous delivery group, but as would be expected a higher percentage of prolonged labours in the forceps group (Fig. 7).

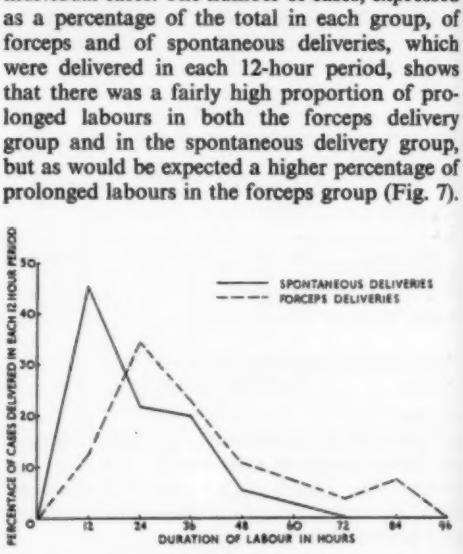


FIG. 7

To show the incidence of prolonged labour in Group B cases.

These results are not unexpected and demonstrate the reliability of the radiological prediction for borderline cases.

THE GROUP C CASES

Group C contains the cases in which there is such a degree of disproportion as to make vaginal delivery unlikely. The majority of cases in this group were delivered by Caesarean section either elective or after a trial of labour. Group C in this series includes cases in which

elective Caesarean section was indicated on grounds of cephalo-pelvic disproportion.

TABLE VI

Group C, 42 Cases or 8·4 per cent of 500 Cases

	Total	Percentage of Total
Number of Cases	42	
Spontaneous Vertex	5	11·9
Vaginal Breech	0	0
Forceps	6	14·3
Caesarean section Vertex	30 } 31	73·8
Caesarean section Breech	1 }	
Not Assessable Elective Caesarean section	19	45·4
Assessable	23	54·8
Correct	18	42·9
Correct plus Elective Caesarean section	37	88·1
Incorrect	5	11·9
Correct as percentage of Assessable Cases	78·3	
Incorrect as percentage of Assessable Cases	21·8	
Correct plus Elective Sections as percentage of Total	88·1	
Incorrect Cases as percentage of Total	11·9	

Nineteen cases were treated by elective Caesarean section and are non-assessable. A second set of percentages have been calculated to include these nineteen cases with the correct cases on the assumption that the prediction of disproportion would have proved correct had it been put to the test.

The inclusion of cases of gross disproportion results in a high proportion of cases in this group being non-assessable.

Those treated by elective Caesarean section are considered to be correct as it is most unlikely that, where both clinical and radiological examination indicate gross disproportion, a trial of labour would result in a vaginal delivery of an uninjured infant.

In the Caesarean section group there were 19 elective Caesarean sections and 13 in which Caesarean section followed a trial labour.

Of the 6 cases delivered by forceps, 2 should have been in Group B and were judged as incorrect. The other 4 were cases of disproportion in the cavity and the amount of difficulty experienced and the length of labours make it clear that in every case a severe degree of disproportion was present. The 5 cases of spontaneous delivery included one primigravida who produced a stillborn baby which at post-mortem showed a considerable subdural oozing of blood. The other 4 spontaneous deliveries occurred in multiparae who had previously given birth to a living baby by the vaginal route. Two were abnormally small babies.

To obtain a spontaneous delivery in a Group C case is possible given good uterine action, a favourable mechanism and a small baby with a considerable degree of moulding. Cerebral injury may occur in some of these cases.

The incorrect forecasts in Group C—5 cases. All 5 cases should have been in Group B. In 1 case there was an error in cephalometry—the radiological measurement being too large.

In 1 case a serious degree of disproportion was shown on the cavity chart alone. It is now known that the cavity chart is unduly pessimistic and it has been redrawn. In 1 case the radiological pelvimetry was carried out when the presentation was a breech. This resulted in a report which was too pessimistic when the presentation became a vertex. The patient had delivered spontaneously her first baby, which was small, as a vertex.

TABLE VII

	Group A	Group B	Group C	Total	Percentage of Total
Number of cases	327	131	42	500	100
Percentage of Total	65·4	26·2	8·4	100	
Not assessable	22	27	19	68	13·6
Percentage of Group	6·7	20·6	45·4		
Assessable	305	104	23	432	86·4
Percentage of Group	93·3	79·4	54·8		
Correct	304	97	18	419	83·8
Percentage of Assessable Cases	99·7	93·3	78·3	97·0	
Incorrect	1	7	5	13	2·6
Percentage of Assessable Cases	0·3	6·7	21·8	3·0	

In 2 cases insufficient allowance was made for the mechanism of asynclitism in a flat pelvis where only the true conjugate was reduced. One of these patients had been delivered by forceps in her first pregnancy.

Conclusion

The figures for the entire series have been summarized in Table VII. This shows the reliability of the predictions based on radiological pelvimetry carried out in cases of suspected disproportion. In 97 per cent of assessable cases a correct forecast was given.

Summary

A series of 500 radiological pelvimetries have been analyzed to determine the value of this procedure in forecasting the course of labour in suspected cases of cephalo-pelvic disproportion.

The radiological predictions were based on Moir's charts. It has been stressed that these charts do not constitute a complete report. Other factors shown on the radiographs have to be considered.

The cases were placed in one of three prognostic groups. The advantage of three groups over five groups has been discussed.

The cavity chart as drawn by Moir was found to be unduly pessimistic and a suggested modification has been described.

A correct forecast was given in 97 per cent of 432 assessable cases.

Acknowledgments

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A REVIEW OF SOME EXPERIMENTAL FINDINGS OF OBSTETRICAL INTEREST

BY

K. J. FRANKLIN, D.M., D.Sc., F.R.C.P.

Professor of Physiology

AND

N. E. WINSTONE, M.B., B.S., D.A., F.F.A. R.C.S.

lately Demonstrator of Physiology

St. Bartholomew's Hospital Medical College, London, E.C.1

PROLOGUE

BETWEEN 1945 and 1947, in the Nuffield Institute for Medical Research, Oxford, a team which included one of us demonstrated a pattern of change of intrarenal blood distribution that occurred in certain pronograde mammals (all of those that were studied showed it) in response to various nervous, chemical, and haemodynamic influences (Trueta *et al.*, 1947). This pattern was an ischaemia of the "cortical" glomerular region (the degree depending upon the number of layers of such glomeruli, from the capsule inwards, that were involved) but not of the "basal" or "juxtamedullary" glomerular one, combined often with hyperaemia of the medulla (more particularly of the corticomedullary junctional region) and dilatation of the renal vein. The researches would have been more complete had blood pressure changes also been recorded, biochemical assessments of renal blood flow, etc., been made, and urine outputs measured. However, the radiographic and structural studies alone provided more than enough problems for solution within two years by the small, and largely part-time, team of five. Also, as has been pointed out elsewhere, renal clearance tests become difficult as oliguria supervenes, and impossible when oliguria changes to anuria.

Since 1947 the same pattern of intrarenal effect has been found under various conditions in all the other laboratory mammals, including the monkey, that have been investigated and Professor E. C. Amoroso (personal communication) also found it in the seal. In the anaesthetized rabbit its production by anoxia can be a dramatic thing to watch, but this effect—which is dependent on intact renal innervation—cannot be a very frequent occurrence in normal life and must presumably be regarded as an emergency reaction (Franklin, McGee and Ullmann, 1951). Löfgren (1951) found paling of the cortex, accompanied by medullary hyperaemia, as a rage response in unanaesthetized cats barked at by dogs, but all the glomeruli were equally affected, and he was unable to get control cats sufficiently at rest to produce pictures equivalent to those secured by Trueta *et al.* (1947) in anaesthetized, unstimulated rabbits (Löfgren, 1954). While the full story in normal animals thus continues to be a desideratum, and a vast literature has accumulated for and against the original statements of Trueta *et al.*, there is no doubt that in certain circumstances the intrarenal blood distribution mentioned can occur in laboratory mammals, and we can say that the major lacuna to date is direct functional evidence in respect of the *human* kidney. That gap, however, may well be closed in the future, for there is a precise parallel between the distribution of the cortical ischaemia seen in certain acute experiments upon animals and that of the damage in human bilateral renal cortical necrosis, and all that appears necessary is an investigative technique suitable to the conditions attaching to direct study of the living human kidney, plus opportunity and permission to employ the technique.

The parallel just mentioned was adequately

stressed in the 1947 book by the Nuffield Institute team. Early in the following year Mr. G. J. Sophian came to one of us (K.J.F.) at St. Bartholomew's Hospital Medical College with his hypothesis relating the occurrence of human "toxaemia" of pregnancy to renal effects produced by over-distension of the uterus.* He had elaborated this view some years earlier; now he specified the basic kidney factor as a change in intrarenal blood distribution such as had been found in the Oxford experiments. Obviously, further animal experiments were not going to prove anything in respect of the human kidney, but the immediate sequel in 1948 was a quick test to see if distension of the uterine cornu of an anaesthetized rabbit would cause renal surface paling. If it were to fail to do so, there would be no indication for further work along such lines. The kidney, however, did so respond, and the results summarized below are in no small measure the outcome of other experiments that followed that first ranging shot, though to some extent they derive from more fortuitous leads. They deal, however, mainly with the rabbit and entirely with laboratory mammals, and objectively we see no scientific justification for any wholesale transference to the human female of effects noted in pronograde mammals that have bicornuate uteri, indulge in multiple conceptūs (15 in one of our does!), and in so many other respects are so different. Oh the other hand, the total findings in respect of the experimental animal are an encouragement rather than the opposite to the belief that Mr. Sophian's hypothesis may be deserving of a clinical test *via* a therapeusis based upon it. While that must necessarily remain a matter for the judgment of the obstetrician rather than for that of the physiologist, we should like to indicate one point of special interest. This is that griping of the immediately puerperal uterus of the rabbit has caused renal effects similar in sign to those produced by distension of the pregnant one. If there is a parallel in the human subject, puerperal "toxaemia" and pregnancy "toxaemia" may be referable, in Mr. Sophian's hypothesis, to a common renal effect; it is our impression that other aetiologies of "toxaemia" fail to account for its occurrence in the puerperium. The factor common to uterine muscle resisting undue distension and to the same muscle contracting and retracting strongly after birth of the litter may be muscular ischaemia and consequent anoxia in the absence of adequate intervals of relaxation and easing of the nutrient blood inflow; this was, we believe, suggested some years ago by Clemetson in respect of the pregnant uterus. It is easy enough to see the blanching which occurs in either case in the experimental animal, but it is not yet known which receptor end-organs are thereby stimulated.

* The prototype of such a view had been advanced by Spiegelberg (1878, 1882) but had thereafter, apparently, been forgotten. Dr. E. Geiringer brought the very interesting section of Spiegelberg's book to my notice in 1952. K.J.F.

The Uterus and Vagina in the Rabbit

Fig. 1 is a scale drawing of these parts in a virgin rabbit; they were fixed in 5 per cent formol saline. The vagina consists of rostral and caudal parts that are functionally dissimilar; they can also to some extent be histologically different, with columnar epithelium near the openings of the cornua and stratified squamous epithelium towards the vulval end.† In dimensions and potential capacity, in our experience, the rostral portion in the mateable virgin is not too grossly different from the same portion at the end of gestation when it receives the foetuses as they are successively passed into it from the uterine cornua.‡ From macroscopic observations at laparotomies, from experiments with smooth muscle stimulants carried out on isolated preparations, and from other indications, it appears that ring contractions can pass from the cornual to the urethral end of this rostral portion, though that is not the whole of the musculature movement story. If the foetus is thereby pushed into the narrow part of the birth canal between the symphysis pubis and the tail end of the spinal column (Fig. 2), reflex contractions of certain skeletal muscles are evoked

† A final report on the epithelium and musculature is not yet available.

‡ Hammond's measurements and figures (Huggett and Hammond, 1952) show much wider variations than those which we have encountered in our Rahere strain of rabbits.

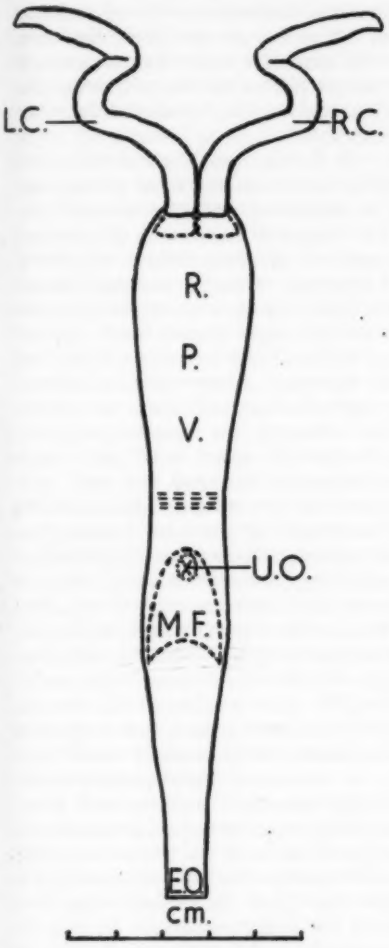

FIG. 1

Dorsal aspect of formalin-fixed uterus and vagina of virgin doe rabbit. L.C., R.C., left and right cornua (vaginal ends shown by discontinuous lines). R.P.V., rostral portion of vagina extending to near U.O., urethral opening, covered by M.F., membranous flap. E.O. external os. Horizontal hatching, markings (? circular smooth muscle) seen on opening up vagina. Scale in cm.

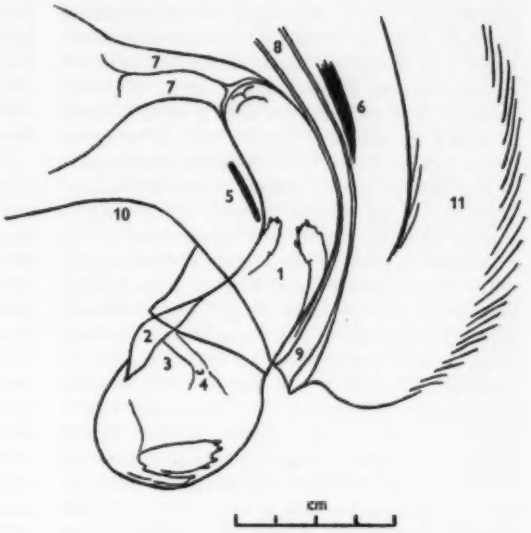

FIG. 2

Foetus and caudal part of birth canal of a doe rabbit. 1, foetus one-third born; 2, placenta; 3, umbilical vessels; 4, umbilicus; 5, symphysis pubis; 6, caudal end of spinal column; 7, empty section of the rostral portion of the vagina contracted down and hence thick-walled after the passage of the foetus through it; 8, smooth colon; 9, anus; 10, mid-line of abdomen; 11, scut. Scale in cm.

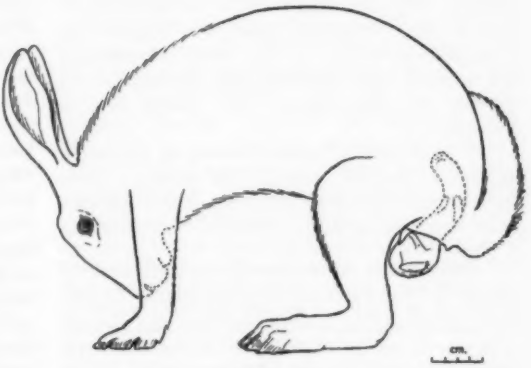

FIG. 3

Natural parturition posture of doe rabbit. Scale in cm.

which together produce the typical parturition posture (Fig. 3) and carry the birth process to completion. It is true that in anaesthetized animals, lying on their sides, there may sometimes be a temporary arrest of the foetus in the caudal portion of the vagina. It is, however, unlikely that such occurs during normal birth in which the stance is upright and the progress of the foetus is fairly, often markedly, precipitate.

The relative lack of change in dimensions and capacity of the rostral portion of the vagina during pregnancy is in striking contrast to the enormous growth of the uterine cornua which, with their contents, constitute at term a large proportion of the body weight and dominate through their activity and requirements the total physiological picture. As an example of such dominance we may cite the arterial pressure fluctuations paralleling the concerted movements of the whole organ. If one lightly palpates the moving mass through the abdominal wall in an anaesthetized, full-term subject, one can say without looking at the record what the arterial pressure is doing; conversely, if one watches the arterial pressure tracing, one can say, so close is the correlation, what the uterus is doing.

Summary of Experimental Results*

Unless otherwise stated, the experimental subjects were doe rabbits and in recent years all that we have personally used have been of our own Rahere strain; in the acute experiments the animals were anaesthetized throughout the periods of observation. The details are as follows:

(1) *Distension of uterine cornua in the virgin subject* (Franklin, 1952). The subjects were laparotomized, the experiments acute. Distension was effected by injection of normal saline at body temperature, by blood conducted from the subject's own carotid artery, by blood conducted from the abdominal aorta of a donor animal, or by blood pumped from the right anterior vena cava of a donor animal, passage of blood in each case being *via* a polythene tube with one end tied into the vessel and the other into the cornu.

Results: (i) Reflex renal cortical ischaemia (abolished by section of the renal nerves) was observed co-terminous with the cornual distension, and varying in degree with the rate and total amount of the fluid inflow. (ii) Renal cortical ischaemia, mediated *via* the adrenal glands (abolished by their exsection or functional exclusion), began slightly later than (i) above and outlasted the distension. There are reasons for doubting an intervention of adrenaline (the main medullary product in the rabbit), though this substance is a renal cortical vasoconstrictor. On the other hand, tests with adrenocorticotrophic hormone and with such corticosteroids as have to date been available have not indicated any particular cortical product as the possible effector agent. (iii) In further acute experiments, distension of either cornu led to arterial blood pressure rises of ± 10 mm. Hg; in a cat the rises were about double this figure.

(2) *Distension of uterine cornua in the pregnant subject.* (i) In unpublished experiments Professor E. C. Amoroso ligated a cornu on either side of an early conceptus, thus preventing it from encroaching (as it normally would have done) in its subsequent development on the no-man's-land between it and the next ones. Some days later, laparotomy under anaesthesia was again performed and the portion of cornu between the ligatures was now so tense that a very slight tap upon it evoked immediate blanching of the kidney surface.

(ii) To judge from observations made in acute experiments upon a series of subjects differing in their times from mating, the kidney surface becomes progressively paler, i.e., renal cortical ischaemia increases somewhat, as pregnancy advances.

(iii) In acute experiments upon full-term (30 days) subjects there was increased reflex paling of the kidney surfaces with the uterine contractions and equivalent regaining of colour with the

* This summary, mainly of results personally obtained since 1948 inclusive, was in large measure orally presented by one of us (K.J.F.) to the International Congress of Gynaecology and Obstetrics in July 1954, and included a number of findings made after the closing date for the despatch of script for the Congress volume. All the essential data have also been presented at meetings of the Physiological Society, members of which have likewise seen the two relevant colour films that were projected in Geneva.

uterine relaxations. Increased intestinal activity went parallel with the bursts of increased uterine activity. As oxytocin in physiological dosage can produce both effects and as it induced parturition in recalcitrant does, it is possible/probable that the increased opposition of the uterine musculature to distension by its contents reflexly acts upon the pituitary gland (compare (8) below) to cause liberation of oxytocin. In that case, the extra paling of the kidney surfaces that accompanied the increased utero-intestinal activity was presumably due to a utero-renal reflex for in physiological concentrations oxytocin, in contradistinction to vasopressin, seems to be without any appreciable direct action upon the cortical vessels. Until the uterine cornua began to exhibit concerted activity, arterial pressure fluctuations were small, but when the organ acted as a whole the pressure rises with contractions increased in size and on occasion approached the order of 20 mm. mercury. As a rule, there was also a small rise in the general level of arterial pressure towards the onset of parturition (Franklin and Winstone, 1954).

(3) *Release of parturient cornua from distension.* In acute experiments with the subjects laparotomized, the kidney surface coloration was seen to become more normal, i.e., the pallor decreased, as successive foetuses were born. In other, non-laparotomized subjects the average arterial blood pressure fell a little during the same period, though it tended to remain somewhat higher at the end of parturition than it had been before labour began.

(4) *Griping of the just puerperal cornua.* In acute experiments on laparotomized subjects, during the hour or so after the birth of the complete litter the cornua were seen to retract in length and contract in cross-section, and to do this so relatively rapidly and forcibly that griping appeared to be an apt term for the process. The arterial pressure was maintained above the pre-labour level and there was a reflex lessening of renal surface coloration that reversed the effect mentioned in (3) above.

(5) *Distension of the rostral portion of the vagina in the virgin subject.* The experiments mentioned in this and the next two sections belong properly to a series designed to test the physiological capacity of the part as affected by the passage of time, with pregnancy as a complicating factor in that passage. In various ways, however, the details are not irrelevant here, and the work as a whole presents useful lines of research in as much as distension of the rostral portion of the vagina has various effects that are also produced by distension of the uterine cornua, and the former does not involve laparotomy except for special purposes.

(i) In acute experiments on subjects that were so laparotomized, distension with a balloon inserted *via* the vulva and then inflated to about the size of a full-term foetus caused rapid paling of the kidney surfaces; the colour returned, though not always at once, on cessation of the distension. Manual compression of the distended rostral portion in one animal caused arterial pressure rises varying in size with the degree of compression. Withdrawal of the inflated balloon to the outside caused "parturition" efforts of skeletal muscles and on occasion was followed for some time by persistence of renal surface pallor.

In another, non-laparotomized animal, of which a colour film record was kindly made for us by Dr. D. A. McDonald, either the balloon was by chance of such a length that the smooth muscle forced it fairly readily into the narrow part of the "birth canal", or the smooth muscle itself was unusually strong and active, or the threshold for reflex evocation of skeletal muscular movements was unduly low, or some combination of these conditions obtained. At all events, "parturition" efforts occurred during the insertion of the uninflated balloon and also while it was being inflated, and subsequent intravenous injection of 0·5 i.u. oxytocin was followed by a series of strong "parturition" efforts (with large rises of arterial pressure and very large ones of intra-balloon pressure) which culminated in "delivery" of the balloon. Except for the shorter duration of the skeletal muscle contractions in the individual efforts, the film record was amazingly like others (also made for us by Dr. McDonald) of normal full-term parturition in anaesthetized does.

In 2 other acute experiments on non-laparotomized subjects the inflated balloon was left in the rostral portion of the vagina for 5 and 6 hours respectively. In the first of these 2

animals more forcible contractions of the abdominal muscles were noteworthy; during the final 2 hours 6 ml. urine at most (instead of a normal 30 ml. or more) were produced by the kidneys and at the subsequent laparotomy the renal cortices were found to be very ischaemic. In the second subject indigo-carmine, intravenously injected after the laparotomy at the end of the experiment, took 6 minutes instead of a normal 1 minute to begin to be visible in the ureter. In neither subject was there structural change apparent in the kidneys on histological examination.

(ii) In each of a series of subjects a balloon was aseptically introduced under anaesthesia and inflated; then the supply tube was detached by a special device and anaesthesia discontinued. The main object was to see what renal effects would be produced within 3 days by a distension equal to that which in acute experiments caused intrarenal blood distribution changes similar to those produced by distension of a cornu. The subjects came out of the anaesthesia fairly rapidly. In one of them the presence of the balloon and, presumably, its intermittent propulsion by the vaginal musculature into the narrow portion of the birth canal caused the subject to adopt the parturition posture time after time (and frequently to micturate) until finally, in just under 3 hours from the induction of anaesthesia, the balloon was precipitately "delivered". In all the other animals the balloons were retained, and over the 3-days period there was reduction of urine output to between 50 and 13 per cent of the normal; in addition, the bladder urine of the most severely affected subject (though of none of the others) contained much protein. There was no change of significance in the blood urea level in such of the animals as were tested. Several, but not all, had ovulated, presumably because the introduction of the balloons had acted similarly to the normal copulation stimuli in this genus. Finally, there were some rather amazing, if sporadically distributed, maturation effects in the mammary glands roughly paralleling in degree in the individual animals the falls in urine output (Aumonier, Franklin and Winstone, 1954).

(6) *Distension of the rostral portion of the vagina in the pregnant subject.* In such subjects also we have introduced balloons and recorded the effects of their presence in the inflated condition as some guide to the properties and activity of the portion of the vagina in question. Though we have done a fair number of such acute experiments on does between 1 and 29 days from mating, we can as yet make merely a reasonable generalization which is, perhaps, an over-simplification of the results. This is that in the first days from mating there appears to be a damping down of the reactions described in the last section, but that from about the 12th day the muscular movements of the rostral portion of the vagina increase in size and frequency, and the reflex evocation of skeletal muscle movements through the entry of the balloon into the narrow part of the birth canal becomes easier and occurs more frequently. In 1 of our 16 subjects, a 23-days pregnant doe, "parturition" efforts led to a rapid "delivery" of the balloon. Two reasons why we must regard the story as at present an over-simplification are (*a*) that we cannot state exactly the parts played by oestrogen, progesterone, etc., and (*b*) we suspect that the number of conceptūs, which even in this series showed very great variation, may be concerned. We were not particularly attentive in this group of experiments to renal effects, but in sighting-shot ones by Mr. Sophian and one of us some years ago progesterone had no obvious effect upon renal surface coloration while oestrogen caused some paling; the results, however, need to be confirmed in a longer series.

(7) *Distension of the rostral portion of the vagina by full-term foetuses during parturition.* The total duration of such distension during normal parturition is often half an hour or less. It seems reasonable to suggest, on the evidence in (5) above, that there is during this time a fall in urine output and a slight extra fillip at the end of gestation to milk formation and possibly (see (8) below) to milk propulsion.

When the distended rostral portion of the vagina forces the foetus into the narrow part of the birth canal, reflex contractions of the diaphragm and abdominal muscles occur, the scut is raised, the back arched, the hind legs are brought more forward under the body and somewhat splayed, and the body as a whole is raised

off the ground by the leg muscles. The forelimbs are extended and slightly abducted, and the head may be bent down between them. In a word, the parturition posture (Fig. 3) is adopted and the powerful aid of skeletal musculature carries the foetus to birth. Even in the anaesthetized subject the average time for the birth of a foetus may be only 2 minutes, and some deliveries can be very precipitate. With each effort there is a temporary rise in arterial pressure. There may be micturition and/or defaecation.

(8) *Distension of the rostral portion of the vagina in the immediate puerperium.* In acute experiments on cats and rabbits Haterius and Ferguson (1938) and Ferguson (1941) found that such distension in the cornual region led to a liberation of 0·5 i.u. oxytocin from the pituitary gland. This dose, according to Cross (1954), is adequate to effect, inter alia, milk propulsion.

In an acute experiment on a doe that had delivered its last foetus only 10 minutes before we began to anaesthetize it, the presence of an inflated balloon in the rostral portion led to "parturition" efforts with arterial pressure rises, and the "foetus" was "delivered" to the extent of projecting 7·5 cm. outside the vulva. Later it was drawn out and re-inserted, and after an intravenous injection of 0·5 i.u. oxytocin it was fully "delivered". Some time thereafter the left kidney was exposed by laparotomy and 0·25 i.u. oxytocin intravenously injected. This resulted in increased intestinal and uterine activity and some paling of the kidney surface. A repetition of the injection after denervation of the left kidney led to paling of the right, but not to any extent of the left, kidney.

Epilogue

From the evidence given above it appears that renal cortical vasoconstriction is present during pregnancy in the rabbit and increases towards full term, but that it is not very marked until perhaps 2 hours or so before parturition, and passes off at about the same length of time after parturition. As haemorrhage also can cause such vasoconstriction (Trueta *et al.*, 1947), that is a possible extra factor to be borne in mind, though in our experience the blood loss during parturition in the rabbit does not seem to be over-great. Except in respect of such occurrence of haemorrhage, we have knowledge of arterial pressure changes that occur simultaneously with the renal vasoconstrictions, and the changes are always increases. If they remain appreciable right up to and within the afferent arterioles, they should be a factor aiding urine formation in the still open glomeruli and thereby offsetting in some measure the urine production drop in the ischaemic ones. On balance we imagine, though we do not know, that there is some oliguria during the few hours' period around parturition, but doubt if the renal vasoconstriction is ever normally long and severe enough to cause proteinuria and renal structural change, though the former did occur in one of our 3-days survival experiments (Section (5) above), and long-continued stimulation of renal nerves (Franklin and Sophian, unpublished) did produce renal structural changes in acute experiments, even in one subject some cortical necrosis. Such strong and lasting stimulation has no parallel, we imagine, in the natural events occurring around parturition time in the rabbit, nor have we found anywhere mention of a "toxaemia" of pregnancy in that genus. It seems to us, therefore, that the mechanisms which produce the renal vasoconstriction should probably be regarded essentially as means by which the kidneys are made to give up part of their large blood flow to the uterus in its need, i.e., that this is merely another instance of their acting as blood-donors (Franklin, 1948) in emergency.

If the human kidneys react by similar cortical vasoconstriction to various uterine stimuli, it is entirely feasible that, when such stimuli are excessive/long-continued and there is a lowering of the excitability threshold in the sympathetic nervous system, the effects may go on from oliguria to anuria, and from proteinuria to bilateral renal cortical necrosis. Our hope is that our experimental evidence may be of some service to the obstetricians who have to decide on the strategy of the campaign against "toxaemia" of pregnancy, and thereby may contribute to a lessened mortality as well as to a lessened incidence of damage among surviving

mothers and children. We are infinitely less concerned (though not, of course, unconcerned) with the additions that the experiments have made to knowledge of pregnancy and parturition in the particular laboratory mammal.

Addendum

Results obtained since this paper was written (October, 1954), and in part communicated to the Physiological Society at its meeting in December, 1954, extend the scope of the survey and in particular give more information about urine output. They cannot be included here as such a procedure would, by etiquette, preclude publication of the full account as an original paper in a journal. But it can at least be stated that they validate and expand, up to the present, the story told in this review.

Acknowledgments

Figures 2 and 3 are reproduced by kind permission of the Editors of the *Journal of Physiology*. For their co-operation in experimental work, the thanks of one of us (K.J.F.) go in particular to Mr. G. J. Sophian, but also to Drs. A. M. Fergusson, P. J. Lindop, J. F. Pearce, and C. Todd, and to Mr. B. R. Wheeler; on the other hand, none of these colleagues is necessarily implicated in any views expressed in this survey. In much of the recent work the histological reports have been essential for the assessment of results, and for these reports we are greatly indebted to Dr. F. J. Aumonier; we also wish to acknowledge various help given by Miss M. E. Morse during the experiments themselves. Nor can we forget the importance of the work of our Animal Technicians, Mr. W. H. Woodcock and Miss M. Butler, who have carried out all the detailed planning and observation necessary to provide us with animals in suitable condition on scheduled dates. In so far as part of the experimental work described comes into a study of the physiology of ageing, it can be regarded as under the aegis of the Nuffield Foundation, to the Trustees of which we offer thanks for a generous grant made towards that study.

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MYOMETRIAL RESISTANCE TO STRETCH THE CAUSE OF PRE-ECLAMPSIA*

BY

JOHN SOPHIAN, M.D., M.R.C.P., F.R.C.S., M.R.C.O.G.

Senior Gynaecological Surgeon
St. Mary's Hospital for Women, Plaistow

THE elucidation of the aetiology of pregnancy toxaemia ranks as the outstanding need in obstetric medicine for upon it depends the rational treatment and the eradication of this dread complication of human attempts at reproduction. The present paper gives a résumé of evidence gathered from many sources and a statement of conclusions based on that evidence.

THE ASSOCIATION OF THE KIDNEY AND UTERUS IN THE AETIOLOGY

In a study of the aetiology an association between the uterus on the one hand and the kidney on the other has gradually emerged. In connexion with the former significance must attach to the common factor of resistance to stretch displayed by the myometrium in the circumstances of primigravidity, of hydramnios, of multiple pregnancy, of concealed rather than revealed accidental haemorrhage, clinical states in which the highest incidence of toxaemia is apparent. The latter reveals itself in the symptomatology. The marked similarity of pre-eclamptic toxaemia to acute nephritis demands emphasis.

The utero-renal reflex (Sophian, 1953) correlates the uterine and renal states.

The suggested renal effect provoked is of the pattern of the renal and intra-renal vaso-motor changes described by Trueta *et al.* (1947). It will be referred to shortly as renal cortical ischaemia (R.C.I.), a designation connoting its chief characteristic. Its occurrence is amply supported by others (Black and Saunders, 1949; Daniel, Peabody and Prichard, 1951, 1952; Daniel, Prichard and Ward-McQuaid, 1954a; De and Sengupta, 1951, 1952; Löfgren, 1951; Solymoss, 1949; Whitcomb and Still, 1954).

My hypothesis postulates that such renal changes are reflexly evoked by the resistance of the uterus to stretch. Considerable further support of this concept in the experimental animal has been provided in the preceding communication by Franklin (1955).

These results also help to explain the peculiar proneness to eclampsia that the pre-eclamptic patient displays at or about parturition. For the first time data are furnished satisfactorily to account for the onset of eclampsia post-partum. The rationalizing of the aetiology has been further served by the recent evidence whereby the effects of the more prolonged distension of the birth canal has comprised the cardinal manifestations of toxaemia.

Mention should be made here that the presence of incipient or established renal vascular disease that forms the background of hypertension or diabetes could enhance the renal response to stimuli of uterine origin and serve to explain the higher incidence of toxaemia in these states.

Difficulties of Proof

At the outset it is well to indicate that direct proof of the thesis is not yet possible for it would require frequent renal angiography. So far as I am aware there are no methods applicable to man which are capable of demonstrating the pattern of the renal circulation. Neither are biochemical methods entirely competent to reveal renal haemodynamics. Selkurt (1954) has recently reported that an exact determination of the glomerular filtration rate is not possible. He

* This paper avoids repetition of Professor Franklin's findings. The reader should therefore have perused it first.

has pointed out that an error of 1 per cent either way in its assessment could be responsible for the daily retention or loss of 11 g. of sodium. An accumulation of this order could easily explain the oedematous manifestation of late pregnancy without revealing its haemodynamic cause. Renal plasma flow estimations require renal vein catheterization in order to serve as accurate indices. No such determinations are as yet available in toxaemia.

Ample evidence exists that R.C.I. is initiated nervously, and that based on clinical evidence the lesser splanchnic nerve can be regarded as providing the principal efferent pathway (Sophian, 1953), though others may exist (vide infra). Chemical poisons, anoxia, shock, a seriously disturbed milieu interieur, as well as stimuli arising from the uterus require an intact innervation to effect the renal change. The purpose of the diversion is two-fold. It may be regarded either as a means of protection of the highly important cortical nephrons against injurious substances transported along their tubules—and here nephron dissections (Oliver, MacDowell and Tracy, 1951), by demonstrating the invariable accompaniment of ischaemic change with the damage caused by poison may be invoked in support, or cortical shut-down, by reducing the renal fraction, may indirectly afford a better oxygen supply to organs where the need arises—to the brain in shock, to the placenta in toxaemia.

Although anticipating the pathological discussion it is important to underline the fact that nephron dissections of the obstetric kidney yielded evidence only of ischaemic damage, a finding of considerable significance that both denies a circulating toxin and supports the aetiological factor of ischaemia, the main contention of the present thesis.

The Uterus

(a) *Uterine tension*

By measuring the intra-uterine pressure changes effected by the sudden introduction of fluid Schultze (1932) determined the distensibility of the human uterus at various periods of the menstrual cycle and the results helped him to plot a "tension curve" which was characteristic of any given woman although it varied with the parity of the individual and the phase of the menstrual cycle.

The primigravid uterus displays an increased resistance to stretch according also to Reynolds and Baker (1951). They have observed that from the 20th week onwards the primigravid uterus responds to the distension of pregnancy by becoming elongated whereas the multiparous organ assumes a spherical form. The former outline connotes a greatly heightened myometrial tension, while the latter indicates a permissive yielding. The significance of this fact is reflected by its synchronizing with the time of onset of pre-eclampsia and by the greater incidence of the disease in the primigravid.

Parviainen and his colleagues (1951) have shown that the uterine tonus is increased in 88 per cent of toxaemias when the blood pressure exceeds 140, while in every case of severe toxaemia it is nearly invariably increased. Toxaemia in the hypertensive only shows such increase in 44 per cent of cases. Mineralocorticoids, together with sodium, tend to increase uterine tone, whilst rest, sodium depletion and ammonium chloride ingestion diminish tone by protecting against mineralocorticoids (Parviainen, 1951). Murphy (1947) has shown that tonus tends to increase in late pregnancy, more so in the primipara than in the multipara. Fulton (1947) has shown that blood pressure increases during labour are due to the increased uterine tonus.

(b) *The effects of tension*

1. *Myometrial ischaemia.* Heightened tension provokes *myometrial ischaemia* (Murphy, 1947; Parviainen *et al.*, 1951; Reynolds, 1950) and becomes responsible for the production of adenosine (Corner and Csapo, 1953). The blood of the toxaemic contains a great excess of this substance (Green *et al.*, 1951) which whilst circulating is capable of additionally provoking reduced glomerular filtration (Houck *et al.*, 1948). Recent experimental evidence indicates that oestrogen accentuates the isometric tension of the myometrium and thereby accounts for the increased production of adenosine (Corner and Csapo, 1953). Wade and Jones (1954) have as a corollary demonstrated that progesterone inhibits human endometrial adenosine triphosphatase. The presence of oestrogen may be held

to influence the supervention of toxaemia in cases of hydatidiform mole, where this hormone could exist in excess.

2. *Placental ischaemia* has been shown to occur in toxaemic and not in normal pregnancy (Browne and Veall, 1953) and can only reflect an ischaemic state of the myometrium which should otherwise offer evidence of congestion because of the high blood pressure maintaining in the general circulation.

Eastman (1954) has emphasized the precarious existence of the foetus towards term and earlier, as a result of its limited oxygen supply. The presence of red streamlines, presumably of oxygenated blood, in the renal vein during the renal blood flow diversion (Trueta *et al.*, 1947) suggests that the considerable amount of blood which constitutes the renal fraction remains under such circumstances more fully oxygenated.

Renal cortical ischaemia by reducing the volume and maintaining the relatively high oxygen saturation of the blood could influence the aeration of the foetus. At the same time the changes it provokes in the kidney will be shown to be responsible for the toxaemic manifestations in the mother.

Uterine ischaemia has essentially been advanced as an aetiological cause by others also (Beker, 1929, 1948; Ogden, Hildebrand and Page, 1940; Bastiaanse, 1949). The taut abdominal wall as a factor has been adduced by Paramore (1932), although he interpreted its effect to be a direct one on the renal circulation —a view recently re-suggested by Bradley (1954).

The Kidney and Pre-eclamptic Symptomatology

(a) *Renal ischaemia and hypertension*

Ample evidence, originally provided by Goldblatt (1948), of renal intervention in the production of hypertension, is to be found in the production of the known hypertensive substance, renin, by renal ischaemia. Even the demonstrations of Grollman, Muirhead and Vanatta (1949) do not exclude the invariable renal origin of such substances, when they demonstrated that the nephrectomized animal, kept alive by the artificial kidney, displayed a raised blood-pressure during survival. Any surgical procedure especially of the extent of bilateral nephrectomy with its accompanying shock must necessarily evoke some degree of renal blood flow diversion. Renal humoral substance thereby produced by the partial ischaemia of the kidney could no longer be destroyed in the absence of the organ. For it has been demonstrated that the Grollman subject in parabiosis with a normal animal loses its hypertension provided the kidneys of the partner are not subjected to ischaemia (Kolff and Page, 1954). Modern therapeusis against hypertension relies for its effectiveness on this principle of effecting the restoration of the blood flow through the organ.

Renal humoral substances comprise renin, vaso-excitor motor substance (V.E.M.) (Shorr and Zweifach, 1949), the products provoked by acute haemorrhage or poisoning (Shipley, Helmer and Kohlstaedt, 1947) and the recently discovered substance pherentasin (Schroeder, 1954). Renin and V.E.M. have been found in excess in the blood of toxaemic patients (Dexter, 1948) whilst in dogs a delayed rise of blood pressure presumably of renal origin has followed the production of acute uterine ischaemia (Beker, 1929, 1948).

In parabiotic experiments renal ischaemia has been found essential for the production of hypertension (Kolff and Page, 1954).

Emotional situations in man will frequently produce a lowering of the renal blood flow which is associated with an elevation of the systolic and diastolic blood pressure (Wolf *et al.*, 1948). It could well be that these occurrences characterize the early days of marriage, contemporaneous with primigravidity and help to aggravate the factors responsible for toxaemia—all acting on the renal blood flow.

Then again Rosenfeld, Thomas and Drury (1954) have drawn attention to certain of their experiments that emphasize the role of the kidney in maintaining hypertension subsequent on cerebral stimulation. They advance an additional nervous pathway responsible for the transmission of the impulses, which comprises sympathetic fibres shown by Kuntz and Alexander (1950) to exist independent of the sympathetic trunks. They consider that failure to recognize their existence when "sympath-

ectomy" has been performed results in only partial denervation of the kidney with consequent limited effect on the reduction of the blood pressure. It may well be that this pathway is responsible for the recovery of vascular tone subsequent to sympathectomy or transection of the cord at levels as high as T.1. Its presence may well be indicated by the effect of apresoline (Stunkard, Wertheimer and Redisch, 1954) in reducing blood pressure under such circumstances for by interruption of the pathway renal ischaemia may be effectively overcome. Stimulation of the renal pedicle influences the production of renin by the kidney (Introzzi *et al.*, 1949) which causes R.C.I. (Daniel, Prichard and Ward-McQuaid, 1954b) and can also result in significant retention of sodium (Berne, 1952; Block, Wakim and Mann, 1952; Surtshin, Mueller and White, 1952). This may contribute to the maintenance of hypertension, as the pressor action of the mineralocorticoids appears to depend on a sufficiency of this salt (Knowlton *et al.*, 1947; Perera and Blood, 1947) which it is believed D.C.A. helps to deposit intra-cellularly possibly to this end (Miller and Darrow, 1941). Renal ischaemia could be invoked if the researches of Hoff and his co-workers (1951) and of Hamburger and Mathé (1952) are integrated. Whilst the latter have shown that alterations in the composition of the extracellular fluid, detectable by freezing point determinations, cause hydration of the cerebral cells with their consequent hyper-excitability evidenced by the epileptic type of E.E.G., the former, by electrical stimulation of the cat's brain produced these vascular changes in the kidney, which if continued resulted in "cortical necrosis". The alterations in the extra-cellular fluid are explicable by renal ischaemia already existing which in turn could be heightened by the excitability of the cerebral cells. Osmotic change can therefore provoke fits. Herein lies the ominous significance of convulsions in the production of anuria.

Byrom (1954) by employing the Goldblatt clamp in the rat has caused a severe progressive hypertension to ensue eventually leading to cerebral damage and to fits. He has displayed the ensuing circulatory changes on the surface of the brain, changes which have been of the nature of acute vascular spasm. They are consequent on the clamping of the renal artery, for its release resulted in immediate visible restoration of the cerebral circulation with contemporaneous cessation of the convulsions. In these experiments based on cerebral vascular spasm the similarity to eclampsia is very close, especially when it has been noted that sudden severe oedema and a more acute onset of encephalopathy could supervene if the animal has previously been fed on salt.

Reduced glomerular filtration rates have been shown to occur in toxaemia (Welsh *et al.*, 1942; Dill *et al.*, 1942; Odell, 1947; Chesley *et al.*, 1940; Bucht and Werkö, 1953; Bradley *et al.*, 1950). Adrenaline and noradrenaline were suspected as the causative agent, but it has been shown that benzodioxane (Assali and Prytskowsky, 1950), effective in producing adrenergic blockade, was without effect on the blood pressure of normal or of toxaemic pregnancy.

(b) *Renal ischaemia and albuminuria*

A severe degree of spasm of the intralobular artery could considerably impair the circulation in the corresponding afferent glomerular vessel and in its capillary tuft. The ischaemia could result in albuminuria. For this is always evident subsequent to anuria in which glomerular stasis invariably occurs. Bradley *et al.* (1950) have shown that the erect posture in acute nephritis diminishes glomerular filtration and increases albuminuria. The 5th Conference on Renal Function of the Josiah Macy jr. Foundation emphasizes the close association of reduced glomerular filtration rates with albuminuria and oedema.

(c) *Renal ischaemia and oedema*

In the production of oedema controversy ranges on the role of glomerulus and tubule. Reduced glomerular filtration supports R.C.I.

Selkurt's observations (1954) that errors in determining glomerular filtration rates are inherent in biochemical deductions and that over a period they could help mask the haemodynamic basis of oedema have already been referred to. Harvey L. White (1950), in animals with an extroverted bladder base and a con-

stricting but not obliterating ligature applied to the renal artery of one side, has found that at the end of a week the kidney appeared to produce only half its normal water and salt output without detectable change in its haemodynamics, whilst the opposite kidney became responsible for making up the deficiency. As both kidneys were exposed to identical humoral influences it is reasonable to assume that no hormone effected this variation. Yet Merrill (1954) claims that, when the normal organ was later removed and the output of the ligated kidney rose to the pre-operative output of the two normal kidneys, without quite equalling their combined filtration rates, the effect was due to an altered response to corticoids by the renal tubules. There is a far greater likelihood that under these unique circumstances of stress there had occurred a haemodynamic change involving a circulation through the juxta-medullary area in addition to the cortex as compensation. Changes in sodium and water metabolism had occurred probably as the result of haemodynamic changes therefore.

Then again Bykov (1947) has demonstrated that dogs conditioned to anti-diuresis, previous to hypophysectomy and consequent development of diabetes insipidus, could still display anti-diuresis on the conditioning stand provided the renal innervation was intact, emphasizing the major part, *vis-à-vis* the hormonal, that haemodynamics play in salt and water retention. The same ascendency is displayed when dogs with diabetes insipidus are deprived of water, for they show a marked reduction in the glomerular filtration rate and in urine flow in consequence (Shannon, 1942). Then again albumen injected intravenously into a nephrotic patient causes a rise of water and salt excretion too immediate for any other explanation than the raised glomerular filtration rate that accompanies it (Lauson, 1950). Glomerular filtration control in the Addisonian patient has been shown by Borst (1952, 1953) to be the only explanation for the diurnal variation of salt and water excretion which still occurs in them. Glomerular changes are evident after the injection of renin (Daniel, Prichard and Ward-McQuaid, 1954b) which in small doses, by reducing the glomerular filtration rate, acts as an antidiuretic (Smith, 1951). Whitney *et al.* (1954) have just shown that both in normal dogs and dogs suffering from diabetes insipidus its exhibition produces a sharp fall in urine volume and a reduction to one-third of the glomerular filtration rate and of the renal plasma flow. Injection of renin results in a significant retention of sodium (Block, Wakim and Mann, 1952; Berne, 1952; Hamburger and Mathé, 1952; Surtshin, Mueller and White, 1952).

Selkurt (1954) asserts "As a corollary it seems unwarranted to conclude that whenever an alteration in $U_{Na}V$—sodium excretion in the urine—occurs in the absence of detectable changes in the glomerular filtration rate a change in endocrine regulation, pituitary or adrenal, is the necessary alternative without more intensive investigation to prove the claim".

Renal cortical ischaemia therefore could be held responsible for oedema.

The Secondary Role of Hormones in Oedema

Attempts have been made to attribute the toxaemic manifestations to alteration in function of the pituitary and/or the adrenal cortex. Anti-diuretic hormone (A.D.H.) is not responsible for the water retention in toxaemia, a fact revealed by the supervention of oedema and other toxaemic manifestations in the patient with diabetes insipidus (Dieckmann, 1953).

Anti-diuretic substance discovered in the urine has also been advanced as a cause. But no attempt has been made to exclude a renal ischaemic origin of such substance for renin can act as an anti-diuretic also, neither has there been an attempt to investigate the effect, if any, it may have on the metabolism of sodium.

Until recently desoxycorticosterone acetate (D.C.A.), a synthetic agent advanced as a corticoid equivalent, has been used in the examination of salt and water retention mechanisms. The nearest counterpart to D.C.A. in the human body shows effects on the excretion of potassium (Sophian, 1953). Aldosterone (Cope and Garcia-Llaurado, 1954; Desaulles, Tripod and Schuler, 1953; *Lancet*, 1953), reported to be a pure salt-retaining hormone, has just been shown by Wettstein and Anner (1954) to possess

"extraordinary sodium-retaining activity with still somewhat greater potassium excretory activity than cortexone".

But potassium losses have not been found to occur in pregnancy toxaemia or in oedema from any cause (Borst, 1953).

Then again, the levels of lipid soluble substance in the urine, a reflection of the corticoid content of the blood, do not correspond with the severity of the toxaemic state (Venning, Singer and Simpson, 1954). Aldosterone can even cause transient sodium loss if exhibited in an Addisonian patient previously treated with D.C.A. (*British Medical Journal*, 1954). Such a dual role implies a regulatory function and appears to characterize corticoid activity.

The corticoids probably marshal the distribution of salt and water between the compartments. It is quite unlikely that the salt-retaining hormone is primarily responsible for the retention in such diverse conditions as congestive heart failure, nephrosis, hepatic cirrhosis with ascites, or pre-eclampsia, where it is claimed to be found (*Lancet*, 1953), for there appears to be no common aetiological factor to provoke its outpouring. Recently Seitchik and Alper (1954) have adduced experimental evidence to show that excessive water retention in pre-eclampsia or in oedematous non-toxaemic patients occurs in the extra-cellular space and that there is no evidence of excessive intra-cellular water retention. Cortical ischaemia could effect this without corticoid intervention. However, aldosterone, while augmenting the urine volume and provoking a transient loss of sodium and chloride in the urine, is found to be responsible for increase in haemoglobin concentration and in the blood non-protein nitrogen representing the disappearance of hydraemia which develops in the adrenalectomized dog treated with D.C.A. (Gross and Cysel, 1954). Dieckmann (1953) has stressed the ominous significance of developing haemo-concentration in impending eclampsia.

But abnormal corticoid secretion as a *primary* cause cannot be reconciled with the non-recurrence of toxaemia in pregnancies subsequent to the first. It will be shown later that conduction anaesthesia and other measures of relieving renal ischaemia are rapidly effective in the treatment of the toxaemic state thereby excluding extrarenal humoral substances—"toxins"—or corticoids, as the prime aetiological factor,

Evidence of R.C.I. from Sodium Excess

The signs of toxaemia are heightened when sodium chloride is retained (Dieckmann, 1953), and the removal of the electrolyte (by cation exchange resin or by exchange transfusion) contributes to recovery in the toxaemic (Carey, 1953) or anuric state (Derot, 1952; Evans *et al.*, 1953). The explanation of the significance of excess of salt in the environment can be afforded by the fact that renal function is suspended when a catadromous fish such as the salmon assumes a salt water existence (Sophian, 1953). A renin mechanism has not been demonstrated in fish. At such times the gills take over the excretory duties which they maintain until the return to fresh water. Based on this the presumable harmful effect of salt on R.C.I. can be assumed in the toxaemic patient. In a very large number of these cases its ingestion causes all the symptoms to mount. Equally significant is the effect of intravenous saline in the anuric (Dieckmann, 1953), in whom R.C.I. maintains, whose first urine when obtainable contains albumen, for the saline provokes hypertension, oedema and convulsions, signs characteristic of eclampsia. Evidence such as this indicates that the harmful effects of salt are based on renal cortical ischaemia.

Salt and Renin Effects Supporting the Thesis of R.C.I. Production

Against this background the recently published work of Renzi and Gaunt (1953) must be considered for the considerable indirect support it provides for my thesis. They "primed" unilaterally nephrectomized rats with D.C.A. and a fluid intake exclusively of normal saline for 30 days. Marked increases in water exchanges occurred together with a mild elevation of blood pressure. On the 30th day a renin preparation was injected for 24–48 hours into one of a paired series. Over half of these cases rapidly developed massive oedema while oliguria, convulsions and death occurred nearly in all. Considerable renal damage was apparent. Angiographic evidence of an R.C.I. mechanism subsequent to renin

exhibition has just been demonstrated by Daniel, Prichard and Ward-McQuaid (1954b). It is apparent that the glomerular ischaemia provoked by renin aggravated the "priming"—be that what it may—produced by D.C.A. and salt, leading to the eclamptic symptomatology and the severe damage the kidneys revealed. Dramatic results were apparent when the second of the pairs in the series had their renin injections interrupted at the end of 24 hours and apresoline exhibited instead. (According to Schroeder (1954), apresoline blocks the effects of renal humoral substances.) Death from renal failure no longer resulted, neither did convulsions continue. The hypertension was reduced. The oedema rapidly vanished and a phenomenal diuresis occurred, whilst the kidneys showed only slight abnormality probably the result of the salt and D.C.A. priming. There can be little doubt that renal ischaemia, revealed by the oliguria/anuria was responsible for the eclamptic syndrome, whilst its relief evidenced by the diuresis accounted for the abolition of the signs and symptoms. These remarkable experiments provide unmistakable evidence of the aetiology, and of the value of treatment when directed to the causative factor—renal ischaemia. They need to be considered side by side with Dieckmann's findings of the result of saline infusions in the anuric in whom cortical shut-down is marked, and in whom a like eclamptic symptomatology is provoked. According to Popják (1944) secondary corticoid influences supervene on the crush syndrome only after 24 hours of its establishment (in its anuric phase) and are in proportion to the crush. Secondary corticoid intervention cannot be excluded therefore in the Dieckmann experiments based primarily on renal shut-down.

Summary of Discussion on Oedema Production

Reduced glomerular filtration rates can effect salt and water retention, so can narrowing of the renal artery (e.g., by ligature). These could result from the Trueta mechanism, which can be provoked by uterine distension. The resistance of the uterus to stretch can be linked to the oedema, albuminuria and hypertension, observed in pre-eclamptic toxaemia. It would, therefore, be reasonable to conclude that the signs of toxaemia of pregnancy are manifestations of an utero-renal reflex. Theobald (1953) in attempting prophylaxis against toxaemia secured remarkable success by denervation of the uterus and indirectly has contributed considerable evidence in support of my thesis. It is also evident that the toxaemic manifestations are heightened by the exhibition of salt, emphasizing the fact that salt can aggravate the underlying pathological state of renal spasm, whilst its removal can contribute to recovery.

The mounting toxaemic process can in certain cases with an unfavourable prognosis show haemo-concentration.

Transfer of extra-cellular fluid to the cells is a possibility, in the absence of diuresis, to explain the haemo-concentration. This has been indicated as an osmotic happening by Hamburger and Mathé (1952). The possible salt and water regulating influence of aldosterone, the new supra-renal salt-retaining corticoid, has been discussed.

The superstructure, if existent, of adrenal intervention in the aetiology is secondary.

Capillary permeability is not the explanation of oedema, as the osmotic tension of the oedema fluid does not reflect it (Dexter and Weiss, 1941; Albano, 1927; Helmuth, 1922; Stead and Warren, 1944; Switzer *et al.*, 1950). But increased capillary pressure due to an aggravation by hypertension may be suspected.

The Pathology as an Aid to Understanding the Aetiology

Sheehan and Moore's summary (1952) of the renal lesions in fatal eclampsia in the young supports the thesis of a renal ischaemia, possibly intermittent, which they consider could afford an explanation for their occurrence.

They affirm that prolonged periods of ischaemia involving the intra-lobular arteries except for their proximal 0·5 to 1 mm. is responsible for the anuric and fatal eclamptic pathology alike. Others confirm that the cortex is ischaemic and the medulla along with the juxta-medullary glomeruli congested in fatal eclampsia (De and Sengupta, 1951, 1952; Solymoss, 1949).

Shaw Dunn and Montgomery (1941) emphasized the escape of the juxta-medullary glomeruli and of the medulla in fatal cortical necrosis. It was on these specimens that Oliver and his co-workers (1951) performed their original dissections and proved the basic ischaemia.

Although renal lesions are either absent or difficult to detect in pre-eclampsia it is a short step in reasoning to incriminate therein a R.C.I. pattern of blood flow redistribution on the basis of the change described in eclampsia and anuria.

The Therapeutic Evidence of an Ischaemic Aetiology and of an Underlying Utero-renal Reflex

The improvement subsequent to overcoming the factor of uterine tension by tapping the amniotic cavity (Barry, 1952, 1954; Smythe, 1949; Feeney, 1953) or by Caesarean section supports the concept of the utero-renal reflex as the mediator in the aetiology. Interruption of nervous impulses arising from the uterus by sympathectomy of the pre-sacral plexus and of the common iliac arteries, the latter chemically by phenol injections of its sheath, has demonstrated its unique value in the prophylaxis of pre-eclampsia (Theobald, 1953).

Direct successful therapeutic attack (Bryce-Smith *et al.*, 1949; Cleland, 1933; Cossutta, 1953; Hingson, 1947; O'Sullivan and Spitzer, 1946; Tuohy, 1951) on renal ischaemia is exemplified by the dramatic improvement effected by conduction anaesthesia reaching the level of the lesser splanchnic nerve, D.10 and 11, especially when combined with ephedrine to produce pavex action. Feeney (1953) and Barry (1952, 1954) have found splanchnic blocking of these segments together with rupture of the membranes of immeasurable value in protecting all cases of concealed accidental haemorrhage against the dread complication of anuria. This so far is unchallengeable evidence in support. They have employed splanchnic block with success in eclampsia also. Further indication of a renal spasm underlying the toxaemic syndrome is provided by the pharmacological action of the newer effective therapeutic agents which help to re-establish the renal blood flow. For it has been shown that the dihydro-ergot derivatives (Barcroft, Konzett and Swan, 1951; Barcroft and Swan, 1953; Blake, 1953; Goetz, 1949; McCall, Taylor and Read, 1953; Mackinnon, 1952) overcome renal ischaemia (Rothlin and Cerletti, 1952, 1954; Rupp, 1953); that veratrone increases the perfusion rate in the isolated kidney (Willson and Smith, 1943) and the renal blood flow in the toxaemic patient (Kaser, 1954); that apresoline, a hydrallazine product, can similarly enhance the renal circulation in laboratory animals and in hypertensive and toxaemic patients (Assali *et al.*, 1950, 1952, 1953; Barry and Geoghegan, 1954; Gross, Druey and Meier, 1950; Moyer, Handley and Huggins, 1951; Renzi and Gaunt, 1953, 1954); that avertin amongst its other effects increases the glomerular filtration rate and promotes diuresis (Brown, Hodges and Bradbury, 1950) —a change for which the others can be equally responsible. Nungesser and Hiatt (1951, 1954) found over a 50 per cent transient increase in effective renal plasma flow following veratrone.

Rauwolfia and hexamethonium help to reduce vaso-spasm. The latter, which has a ganglion-blocking effect, has been shown by Candiani (1953) to have a beneficial effect on renal function particularly when a convulsive attack is imminent, for it causes an increase in the glomerular output. The former is employed in the reduction of blood pressure because of its action on vaso-motor centres in the brain. Its primary pharmacodynamic effects on the kidney have not been investigated but relief of renal spasm may result from its cerebral effects (vide supra).

Both apresoline and veratrone increase the renal blood flow. They are held to exert their influence centrally on mid-brain or medulla.

Pathways exist other than the normal sympathetic ones (Kuntz and Alexander, 1950) to convey this central impulse to the peripheral blood vessels, which ganglionic blocking cannot interrupt. This is also evident in the action of apresoline. Both these substances enhance the renal blood flow when producing their hypotensive effect and it would be reasonable to adduce from the previous afforded evidence that the reduction of hypertension accompanying their use results from their action in overcoming renal ischaemia, thereby helping in the

destruction of renal humoral substance. Adrenergic blockade is of no value in the therapeusis of the toxaemic state (Assali and Prytskowsky, 1950). This finding denies to adrenaline or noradrenaline any share in the aetiology of pre-eclampsia.

Sauter (1949) claims to benefit the toxaemic state by the employment of hydro-ergot derivatives that overcome uterine tonus—a support of my thesis.

The problem of toxaemia is the problem of renal ischaemia and the uterine stimulus giving rise to it.

Dietary sodium restriction or sodium depletion by resins to curtail the environmental stimulus to the kidney; rest in bed to reduce the renal vascular sensitivity to stimulation; methods aimed at securing diuresis by hypertonic glucose (Tatum and Mule, 1954), by inhibiting the activity of carbonic anhydrase, or by variation of the pH of the plasma; all provide a flank approach to the therapeutic problem. So do exchange transfusions in securing an optimum milieu to assist the renal function.

From all this it could be inferred that the utero-renal reflex demonstrated in animals has its counterpart in the human being; that it is responsible for pre-eclamptic toxaemia, eclampsia and anuria, at least in the obstetric patient. Successful therapeusis along the line of attack on the effector or on the target organ or on the intermediate nervous pathway supports my thesis. No corticoid or toxin could be affected by the treatment outlined, no supra-renal hormone, if primarily responsible for toxaemia, would fail to repeat its effects in subsequent pregnancies.

Summary

The almost complete identity of the signs of acute nephritis and those of pre-eclamptic toxaemia indicates a renal basis for the latter as well.

Pre-eclampsia occurs in those women whose uteri are resisting excessively the normal or abnormal stretching influences of pregnancy.

In animal experiments stretching of the uterus reflexly produces renal blood flow redistribution of the type described by Trueta *et al.*

This redistribution is characterized by a narrowing of the renal artery and a progressive shut-down of the intralobular arteries and their afferent glomerular branches from the capsule inwards, and proximal portions of the intralobular arteries together with their branches to the basal or "juxtamedullary" glomeruli escaping the constriction. "Cortical glomerular" ischaemia results.

Salt and water retention can occur independently of excess in tubular reabsorption as the result of spasm of the afferent glomerular arterioles. So can hypertension and albuminuria.

"Cortical" ischaemia with "juxtamedullary" escape is to be inferred as occurring in toxaemia from the renal histology of anuria and of eclampsia.

Therapeutic measures successful in overcoming renal ischaemia have proved of value in the treatment of the pre-eclamptic, eclamptic, and anuric states.

It is reasonable to conclude that pre-eclampsia, eclampsia, and anuria are evidence of renal ischaemia of the type described by Trueta *et al.* and are evoked by the resistance of the uterus to stretching. If this conclusion is accepted it follows that prophylaxis and treatment, to be effective, must be directed to interference with the utero-renal reflex either at its receptor or at its effector end, or at some point in the intercalated nervous pathway.

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A CLINICAL STUDY OF PRE-ECLAMPSIA

Part I

BY

T. R. NELSON, M.B., M.R.C.O.G.

Senior Registrar

Aberdeen Maternity Hospital

INTRODUCTION

PRE-ECLAMPSIA, which has long exercised a fascination for obstetricians and others, has been responsible for a great amount of research work and the accumulation of a vast literature. The lack of any true knowledge of its cause holds out a further challenge, and the literature abounds with theories and reports of laboratory work which attempt to illuminate or solve its basic nature.

Little attention has been paid to the epidemiological method of research, and, while this may not yield any fundamental facts about aetiology, it seems possible that information about the frequency of the condition and some of the factors influencing it might give some useful pointers. This paper is concerned with this aspect of the subject, and the effect of various demographic factors will be assessed. The problem of the epidemiology of the disease itself will be considered first and, in a subsequent paper, a similar type of analysis will be applied to the two complications, eclampsia and foetal death. Where appropriate, the implications of these findings upon treatment will be mentioned.

Clinical Material

As it is well known that parity influences both the incidence and effects of pre-eclampsia, it was decided that this investigation should be restricted to first pregnancies. In this way diagnostic confusion is also restricted, for the vascular-renal lesions, the anaemias, and the other processes which may mimic pre-eclampsia are probably less common in primigravidae than in multigravidae. Cases of multiple pregnancy were also omitted to simplify analysis for it is known that they carry an increased risk.

Every case record of booked primigravidae confined in the Aberdeen Maternity Hospital from the time of the opening of the new hospital in 1938 up to and including 1953 has been examined, and on the evidence available a diagnosis of the presence or otherwise of pre-eclampsia has been made.

The records of the booked primigravidae, married and resident in the City of Aberdeen (B.M.C.P.), were for some purposes analyzed separately. This group is subject to the minimum effect of selection since about 85 per cent of all the city primigravidae are delivered in the Aberdeen Maternity Hospital.

Consideration of the diagnostic criteria for an investigation of pre-eclampsia leads immediately on to highly controversial ground, for it is difficult to devise a definition of pre-eclampsia which will meet with general approval. The following brief statement is not intended to cover all the points which might be argued, but outlines the principles followed in this investigation.

Diagnostic Criteria

Pre-eclampsia is typically a disease of the last trimester of pregnancy, and the 26th week is taken in this study as the dividing line. It should abate with the cessation of the pregnancy, but the imposition of a time limit for this is not rigid.

Mild Grade. With or without oedema, the blood pressure (diastolic) rises to 90 or more on two or more occasions separated by at least a day, or shows a definite or progressive pattern if the rise occurs in labour. The readings should not be so separated that a definite relationship cannot be inferred. This hypertension occurs in the absence of albuminuria.

Severe Grade. In the presence of a raised blood pressure which satisfies the above criteria, albuminuria raises the grading to severe. Where possible, estimations on catheter specimens of urine are taken in preference to those in non-catheter specimens. Readings on the Esbach's scale of ¼-part/1,000 or less, or observation that a "trace" of albumen was present in a non-catheter specimen, have been disregarded, particularly if made on isolated occasions. Such cases are graded "mild" if the blood pressure warrants this.

Oedema has been omitted as a factor for both grading and diagnosis.

Eclampsia may be defined as a convulsive state occurring in pregnancy, in which epilepsy and other obvious causes of the convulsions may be reasonably excluded. In no case in this series did eclampsia occur without previously recognizable pre-eclampsia. For reasons which will be gone into in a subsequent paper, cases of eclampsia have been included under the grading of the previously existent pre-eclampsia, and not automatically as severe pre-eclampsia or in a separate category.

The hypertension of pre-eclampsia has now been generally accepted as diastolic in nature, and the selection of the figure 90 as the lower limit of abnormality is, of course, entirely arbitrary, being a compromise between clinical experience and practice and the dictates of the investigation. Any attempt to delimit "normal" blood pressure is bound to be a matter of argument and speculation; and up to the present there has been no real and incontrovertible evidence to establish the correct answer to the question.

A degree of unreliability must obviously be expected where a single sign alone (as, in the case of mild pre-eclampsia, blood pressure) bears the full responsibility of diagnosis, even when the field is narrowed down by the obligatory presence of pregnancy.

Oedema is often regarded as part of the pre-eclamptic syndrome. While there is no question of failing to diagnose the severe grades in the lower limb, the minor grades present difficulty, and White (1950) has shown that the volume of the leg must increase by about 8 per cent before oedema becomes clinically manifest. Furthermore, oedema in the lower limbs is frequently found in association with normal pregnancy, and is thought to be due to mechanical causes. Recognition of anything but gross oedema in sites other than the lower limb is even more difficult. As there is no satisfactory way of assessing degrees of oedema, its presence or absence has not been used for either diagnosis or grading.

Several other factors have been purposely omitted from the grading criteria. For instance, the duration of the disease and/or the swiftness of its development. The further from term that pre-eclampsia develops, the more difficult do these two points become in assessment. Obviously, when the patient is being seen at intervals of a fortnight or more, as, for instance, between 26 and 32 weeks, pin-pointing the clinical onset of pre-eclampsia must be far from accurate. Therefore the use of this factor would not be very helpful.

The minimum rise of the blood pressure required for diagnosis has been mentioned. The upper limits reached by any individual case have not been used. One of the outstanding characteristics of the pre-eclamptic blood pressure is its extreme variability, even under apparently basal conditions. Such variability is unsatisfactorily expressed in terms of a single reading.

It should be stressed that, although certain features of pre-eclampsia have not been used for the present purposes, the importance of these in practice is not denied. The matter at issue is the design of an easily applicable set of diagnostic rules.

It will be appreciated, therefore, that this series is composed, as far as a retrospective investigation can ensure, of cases of the true pre-eclamptic syndrome alone, and does not include the full range of what are often described as the "toxaemias of pregnancy". No case has been included where pre-eclampsia might be diagnosed as having complicated the course of previously existent essential hypertension.

The rigidity and extreme simplicity of the criteria may be questioned. However, any investigation such as this, which is almost entirely retrospective, must be kept to a simple set of rules which can be rigidly applied so that

there is no temptation for the investigator to use his "judgment". The latter may change during the course of the enquiry and lead to inconsistencies of diagnosis and grading.

It would be of interest to compare the incidence of pre-eclampsia in various areas, but the difficulties are great. In addition to the questions of definition and the standards of routine recording at antenatal clinics, there is the very important factor of selection. It is felt that many of these shortcomings are minimal in this instance, and that the figures to be presented are approximately true statements of the incidence of mild and severe pre-eclampsia in the primigravidae of Aberdeen during the period 1938–1953.

The Incidence of Pre-eclampsia and Eclampsia

About a fifth of all booked primigravidae from 1938 to 1953 had a rise of blood pressure, warranting the diagnosis of pre-eclampsia: this was mild in 18·9 per cent of cases and severe in 4·6 per cent. Eclampsia occurred in 0·5 per cent, or once in 193 cases.

To study any possible change in incidence, the whole 16-year span was divided into 5 roughly comparable sub-sections. These sub-sections are also convenient in that they demarcate certain landmarks in the hospital's expansion, and in the policies governing the treatment of pre-eclampsia. The divisions were as follows:

1938–1942. Hospital mainly for lying-in patients.
1942–1945. Antenatal hospital and special prematurity nursery in full operation.
1946–1947. Mainly characterized by the great increase in the birth rate which occurred at the end of the war.
1948–1950. Heavy sedation used readily in the treatment of severe pre-eclampsia and eclampsia.
1951–1953. Aberdeen Maternity Hospital confines almost the whole of the married city primigravid population.

Table I gives the incidence of pre-eclampsia and eclampsia during these years. It shows that the incidence of eclampsia, having remained at a constant figure of 0·8 per cent during the first 10 years, gradually declined after 1948, until now it is almost a quarter of the previous incidence, that is 0·3 per cent or 1 case in 398 primigravidae. (In 1952 and 1953, the incidence was 0·2 per cent, or 1 case in 538 primigravidae.) This decrease has not been paralleled by a decrease in the incidence of severe pre-eclampsia. On the contrary, the incidence of the latter has increased during the same period, that is, from 2·9 per cent in 1946–1947 to 6·8 per cent in 1951–1953. The fact of this increase may be stressed for it has occurred despite increasingly strict standards of antenatal care.

The figures for mild pre-eclampsia show a rather unexpected rise in the years 1946 and 1947, which is quite out of keeping with the incidence in the other 4-year groups. Disregarding this rise for the moment, it would appear that mild pre-eclampsia has gradually increased in incidence. These figures, however, must be interpreted with the greatest care, for blood pressures were not recorded in 1938–1942 as frequently as at present, and therefore there is

Table I

Incidence of Pre-eclampsia and Eclampsia during the Years 1938–53
(All booked Primigravidae. Percentages in brackets)

Years	Eclampsia	Severe*	Mild*	Total Primigravidae
1938–1942	21 (0·8)	86 (3·2)	352 (13·2)	2,669
1943–1945	14 (0·8)	53 (3·0)	279 (15·4)	1,814
1946–1947	14 (0·7)	60 (2·9)	730 (35·4)	2,060
1948–1950	12 (0·4)	174 (5·5)	550 (17·3)	3,182
1951–1953	8 (0·3)	216 (6·8)	527 (16·6)	3,183
Total 1938–1953	69 (0·5)	589 (4·6)	2,438 (18·9)	12,908

* Cases of Eclampsia included according to pre-existent Pre-eclampsia.

now a proportionately greater opportunity to record transient phases of hypertension than previously. Furthermore, as will be shown later, mild pre-eclampsia is influenced greatly by age, and therefore the overall incidence in any group of primigravidae will depend on the relative proportions of young and old.

The phenomenon in 1946–1947 may be partly explained by the fact that at this period, because of the great increase in the numbers of patients resulting from the high post-war birth rate, blood pressures were taken by pupil midwives, often rather hurriedly and with the patient sitting. The readings were not checked by the medical staff unless the patient showed other signs of pre-eclampsia. Now, all blood pressures are taken by the medical staff with the patient lying relaxed upon the examination couch.

If the bizarre figure in the years 1946–1947 is in fact due to this circumstance, it illustrates one of the pitfalls of investigations of this type when observations are made by many workers, in varying conditions. Nevertheless, the figures quoted in Table I appear to be reliable in every other respect.

From 1948 onwards, the figures, within the definitions laid down, probably represent the true incidence of mild pre-eclampsia in the Aberdeen primigravid population. The inclusion of twin pregnancies would not alter this figure greatly because of the infrequency of twinning in primigravidae.

From the figures quoted, eclampsia can be recognized as a preventable disease since its incidence decreases with improved therapy. Severe pre-eclampsia, on the contrary, has increased despite the improvement in antenatal care. In this series at least, all the efforts spent in early diagnosis and treatment have not helped to decrease the incidence of either severe or mild pre-eclampsia.

The Effect of Age upon the Incidence of Pre-eclampsia

Severe Pre-eclampsia

As the accuracy of the diagnosis of severe pre-eclampsia can be relied upon with fair certainty even in the early years of the investigation, the whole series may be used to study the effect of age upon this grade of pre-eclampsia, and Table II shows this analysis.

It will be seen that the incidence of severe pre-eclampsia varies very little with age in this large series. If smaller numbers are taken, one finds inconsistent and variable results. Probably this is the reason for previous writers stating that either young or old primigravidae were particularly prone to pre-eclampsia. It is suggested that this large series is fairly authoritative in demonstrating that all ages are equally prone to the disease.

Mild Pre-eclampsia

Owing to the objections made previously, the effect of age upon the incidence of mild pre-eclampsia can only be demonstrated in the last 6 years. Here it is most accurate to consider only the booked married city primigravidae, since those booked patients coming from the country districts did not have their blood pressures taken so often at the clinic.

Table III demonstrates the analysis by age. Under 30 years of age the incidence remains fairly constant, but there is a striking increase in incidence over this age. In the age group 35 years and over, the incidence is about twice that of the under twenties.

Table II

Age and Severe Pre-eclampsia

Under 20		20–24		25–29		30–34		35+		Total	
No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
76 / 1,741	4·4	264 / 6,335	4·2	169 / 3,107	5·4	56 / 1,077	5·2	24 / 501	4·9	589 / 12,908	4·6

All Booked Primigravidae, 1938–1953. Eclampsia included according to pre-existent Pre-eclampsia.

TABLE III
Age and Mild Pre-eclampsia

Under 20		20–24		25–29		30–34		35+		Total	
No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
86 / 644	13·4	421 / 2,731	15·4	202 / 1,313	15·3	94 / 400	23·6	47 / 163	28·2	849 / 5,251	16·2

Booked Married City Primigravidae, 1948–1953. Eclampsia included according to pre-existent Pre-eclampsia.

Contrary to the findings in severe pre-eclampsia, the incidence of mild pre-eclampsia rises sharply after the age of 30. Since this is also the age at which essential hypertension begins to show itself to any extent in women (Robinson and Brucer, 1939), the question arises as to whether this rise is due to true mild pre-eclampsia or whether pregnancy has simply "brought out" latent hypertensive tendencies.

Figure 1 shows the percentages graphically for both mild and severe pre-eclampsia (B.M.C.P.). It shows that until the age of 30 the lines depicting mean incidence run parallel; and there seems no valid reason why they should not continue to do so. If this were true, the excess incidence over that expected may be due to latent essential hypertension becoming manifest under the conditions of pregnancy. Some method of distinguishing between these two processes, therefore, is required.

Furthermore, whether this suggestion is true or not, the evidence suggests that the com-

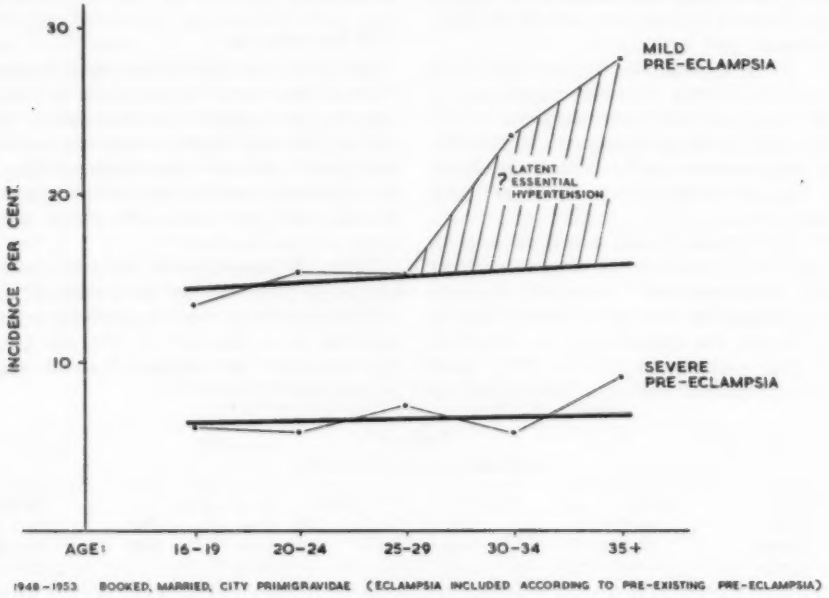

FIG. 1

Graphic demonstration of incidence of mild and severe pre-eclampsia. Heavy straight lines represent visual means; see text for fuller explanation.

position of the mild pre-eclampsia group is complex and not necessarily the same as the severe group. Therefore, the temptation to add mild cases to severe in order to increase the total numbers available for study must be strongly resisted.

The Effect of Social Class upon the Incidence of Pre-eclampsia

The social classification devised by the Registrar General has been found to be very useful in social-medical research, and many diseases have been found to have a definite social class gradient. So far as pre-eclampsia is concerned, if any social class difference in incidence or severity was discovered this might be presumed to act through differences in physique, health or diet, or through differences in standards of antenatal care. Thomson (1954) in an extensive dietary survey of pregnant women in Aberdeen found differences in quantity and quality of diets between the social classes.

To establish the relationship between pre-eclampsia and social class, all booked married city primigravidae in the years 1948–1953 were studied, for complete social data is available for this group. Table IV gives the incidence of severe pre-eclampsia by age and social class. It shows that there is a slightly greater incidence in Social Classes I and II than in IV and V. This is probably accounted for by the fact that in this particular series, at least, there is a tendency for the incidence to rise slightly with age; and there are more elderly primigravidae in Social Classes I and II than in the other social groups. Age for age, however, there is no obvious social class difference in incidence.

Table V shows the same information for mild pre-eclampsia. Once again, taken age for age, there is no social class gradient, though the overall figures might suggest a lesser frequency in Social Classes IV and V.

Although this series is rather small, it is probably safe to say that the social class effect, if any, is slight, and that under conditions existing in Aberdeen at least, the risk of developing severe pre-eclampsia is practically the same in all social classes. This does not give any positive evidence to eliminate diet as an important factor in the genesis of pre-eclampsia: but rather, it suggests that the factors implicit

Table IV

Social Class and Severe Pre-eclampsia

Social Class	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
I and II	2/11	18·2	5/159	3·2	16/203	7·9	8/79	10·1	3/26	11·5	34/478	7·1
III	23/380	6·1	111/1,704	6·5	71/867	8·2	10/245	4·1	9/110	8·2	224/3,306	6·8
IV and V	14/253	5·1	41/863	4·7	12/242	5·0	5/74	6·8	3/27	11·1	75/1,459	5·1
Social Class not stated	—		5		1		2		—		8	
All Classes	39/644	6·1	157/2,731	5·8	99/1,313	7·5	23/400	5·8	15/163	9·2	333/5,251	6·4

Booked Married City Primigravidae 1948–1953.

TABLE V

Social Class and Mild Pre-eclampsia

Social Class	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
I and II	1/11	9·1	24/159	15·1	30/203	14·8	18/79	22·8	9/26	34·6	82/478	17·2
III	53/380	14·0	289/1,704	17·0	139/867	16·0	56/245	22·9	30/110	26·4	567/3,306	17·2
IV and V	32/253	12·7	107/863	12·4	33/242	13·6	20/74	27·0	8/27	29·6	200/1,459	13·7
Social Class not stated	—		5		1		2		—		8	
All Classes ..	86/644	13·4	421/2,731	15·4	202/1,313	15·3	94/400	23·6	47/163	28·2	849/5,251	16·2

Booked Married City Primigravidae 1948–1953.

in social class, one of which is diet, do not exist in sufficient range in Aberdeen to show any effect upon the incidence of either mild or severe pre-eclampsia.

THE EFFECT OF HEIGHT UPON THE INCIDENCE OF PRE-ECLAMPSIA

Baird (1949) has previously published evidence that tall women (5 feet 4 inches and over) have lower foetal mortality and prematurity rates than small women (under 5 feet 1 inch). This is thought to be the indirect effect of social class; that is, Social Classes IV and V (in Aberdeen at least) contain about 5 times as many small women as Social Classes I and II. It is presumed that the excessive number of small women in the lower social classes is the result of faulty home conditions and defective diet during the growing years. Furthermore, it has been shown by Thomson (1954) that many of these small women carry over their poor dietary habits into pregnancy.

It was thought, therefore, that a study of the influence of height upon the incidence of pre-eclampsia would be worth while in that it would be a check on the negative findings of the social class analysis.

Table VI shows that severe pre-eclampsia is almost as common in tall women as it is in small. Analysis within individual age groups shows that the overall figures probably are not of any great significance, and no convincing effect of height can be demonstrated. In Table VII, it will be seen that the incidence of mild pre-eclampsia, age by age, is not convincingly affected by height. The tall women appear to be, over all, slightly more prone to mild pre-eclampsia that the other two groups, but this is because there are relatively more tall women over 30 years.

These findings substantiate those of the social class analysis and are essentially negative.

RELATIONSHIP OF EXCESSIVE WEIGHT GAIN TO PRE-ECLAMPSIA

Several analyses have been made of the variations and means of weight gains during pregnancy, but there is no agreement as to what the normal or ideal should be. Lack of any true knowledge of the physiology of pregnancy makes

TABLE VI

Severe Pre-eclampsia and Height

	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Tall	3/126	2·4	34/679	5·0	25/394	6·3	5/138	3·6	5/43	11·6	72/1,380	5·2
Medium	23/328	7·0	84/1,359	6·2	50/633	7·9	14/186	7·5	4/69	5·8	175/2,575	6·8
Small	13/181	7·2	39/676	5·8	24/274	8·8	4/74	5·4	6/51	11·8	86/1,256	6·8
Height not stated	9		17		12		2		—		40	

Booked Married City Primigravidae, 1948–1953. Eclampsia included according to pre-existent Pre-eclampsia.

it difficult to deduce the nature of an ideal weight gain. In this investigation it was decided to check the statements made by Hamlin (1952), that women, and primigravidae in particular, who gained more than 8 pounds during the period 20 to 30 weeks were at marked risk of developing pre-eclampsia, which if not dealt with adequately would progress to eclampsia.

A selection was made from the booked married city primigravidae on the following lines. All cases in three consecutive years were taken, and from these, those whose weights were known at the 20th week were selected. This group was then divided into three sub-sections:

(*a*) Those who developed severe pre-eclampsia.
(*b*) Those who developed mild pre-eclampsia.
(*c*) Those who had no pre-eclampsia, and who had no pathology during pregnancy such as late vomiting, hydramnios, or stillbirth, etc., which are likely to affect weight gains. It was decided to make this group, as far as possible, representative of efficient childbearing.

The remaining cases have been excluded from the present investigation as they are likely to be composed of a heterogeneous group of excess and minimal weight gains: they are, however, numerically small.

A total of 1,457 cases were thus available for investigation, 216 of which were mild pre-eclamptics and 126 were severe pre-eclamptics. The mean weight gain for the period 20 to 30 weeks was 10·3 pounds for normal pregnancies, and 12·2 pounds for both mild and severe pre-eclampsia.

About two-thirds of the normal pregnancy group and three-quarters of the pre-eclampsia groups came into the 8 pounds or over category. Since the mean weight gain was 10 pounds in this series, it was decided to make a division at the 10-pound level, and thus divide the normal pregnancy group into two roughly equal sections. The results are shown in Table VIII.

It is clear that there is a tendency for those who will later develop pre-eclampsia to gain excessively in the 20–30 week period. Nevertheless, more than half the normal cases gained excessively, and approximately one quarter of the cases of pre-eclampsia were in the lesser gain group.

Table IX shows a more detailed analysis by age groups. It will be noticed, in particular, that of the women over 30 years of age, who developed severe pre-eclampsia, about half gained less than 10 pounds in the 20–30 week period. In the 3 years used for the analysis there were 25 cases of severe pre-eclampsia (B.M.C.P.) over 30 years of age, and of these 22 reported to the clinic before the 20th week of pregnancy. Only 12 of these 22 gained more than 10 pounds in the critical period. These numbers are unfortunately small but the findings are of great significance, for, as will be shown in a subse-

TABLE VII
Mild Pre-eclampsia and Height

	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Tall	15/126	11·9	118/679	17·4	71/394	18·0	35/138	25·4	10/43	23·3	249/1,380	18·0
Medium	45/328	13·7	206/1,359	15·2	88/633	13·9	44/186	23·5	22/69	31·9	405/2,575	15·7
Small	26/181	14·4	94/676	13·9	41/274	15·0	15/74	20·3	15/51	29·4	191/1,256	15·2
Height not stated	9		17		12		2		—		40	

Booked Married City Primigravidae, 1948–1953. Eclampsia included according to pre-existing Pre-eclampsia.

TABLE VIII
Weight Gains in the 20–30 Week Period
(Percentages in brackets)

	Under 10 pounds		Over 10 pounds	
Normal Pregnancy	485	(43·4)	631	(56·6)
Mild Pre-eclampsia	62	(28·6)	154	(71·3)
Severe Pre-eclampsia	34	(27·0)	92	(73·0)

TABLE IX
Weight Gains: 20–30 Weeks
Booked Married City Primigravidae, 1949–1951

Age	Weight Gain	Normal Pregnancy Per cent		Mild Pre-eclampsia Per cent		Severe Pre-eclampsia Per cent	
Under 20	Under 10 pounds	51·8	(110)	37·5	(24)	33·3	(12)
	Over 10 pounds	48·2		62·5		66·7	
20–24	Under 10 pounds	42·5	(602)	27·5	(109)	25·0	(60)
	Over 10 pounds	57·4		72·4		75·0	
25–29	Under 10 pounds	42·4	(304)	28·0	(50)	15·6	(32)
	Over 10 pounds	57·6		72·0		84·4	
30+	Under 10 pounds	43·0	(100)	27·0	(33)	45·5	(22)
	Over 10 pounds	57·0		73·0		54·5	

Figures in parenthesis refer to total of cases in each age and pregnancy group.

quent paper, the high stillbirth rate in severe pre-eclampsia is due almost entirely to the excessively high rate in those over 30 years of age. In this group, requiring the greatest help, the prognostic value of weight gains is unfortunately of very little value.

To sum up, and from a practical point of view, out of every 1,000 primigravidae in Aberdeen, about 60 will develop severe pre-eclampsia; 45 of these would gain more than 10 pounds in the 20–30 week period, while 15 would gain less. Were we to apply Hamlin's criteria and on the basis of his work apply dietary control, we would need to do so in 500 women to influence the prognosis in 45, whilst the remaining 15 severe pre-eclamptics would not be included.

Furthermore, the application of dietary control would be unlikely to have much effect upon the stillbirth rate, for half of those over 30 years of age who are to develop severe pre-eclampsia would not satisfy the criteria for its application. And it is over the age of 30 that the risk of stillbirth is highest.

Summary

(1) Severe and mild pre-eclampsia, under the present definition, may not be the same disease, particularly over the age of thirty.

(2) The incidence of mild, but not severe pre-eclampsia, increases sharply over the age of thirty.

(3) The incidence of pre-eclampsia is the same in all social classes.

(4) The incidence of pre-eclampsia is not affected by the height of the patient, and, therefore, probably not by the physical development and general health.

(5) Excess weight gain during the 20 to 30 week period of pregnancy is associated with a higher risk of severe pre-eclampsia but only under the age of 30. At all ages, there is an increased risk of mild pre-eclampsia if weight gain is excessive.

(6) The relationship of weight gain to pre-eclampsia, and in particular the severe grade, is too indefinite to be of real practical value in predicting the development of pre-eclampsia; and dietary control is, in fact, unlikely to benefit those who require help most.

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A CLINICAL STUDY OF PRE-ECLAMPSIA

Part II

BY

T. R. NELSON, M.B., M.R.C.O.G.

Senior Registrar

Aberdeen Maternity Hospital

IN a previous paper (Nelson, 1955) the epidemiology of pre-eclampsia as a disease was studied, and analyses were made to determine the influence of various factors. In this paper, the same clinical material is used, with the same criteria for diagnosis and grading. Two of the main complications of pre-eclampsia—eclampsia (with maternal mortality) and death of the foetus—are considered and an assessment made of their frequency and importance.

A. THE COMPLICATIONS OF PRE-ECLAMPSIA: ECLAMPSIA

The Problem of Eclampsia

Eclampsia, the most dramatic danger of pregnancy and labour, has had focused upon it almost more attention than any other complication. Its actual relationship to pre-eclampsia has not, however, been clearly defined. The concept, implicit in the names used, that eclampsia is a direct or logical outcome of a severe stage of pre-eclampsia has been reiterated by Hamlin (1952) and Dawson (1953) within recent months. This logicality is not acceptable in the face of clinical experience for it is well known that convulsions may supervene upon a case of mild pre-eclampsia, while a very severe case may escape. There is much to recommend the view which regards eclampsia in the light of other convulsive episodes (Rosenbaum and Maltby, 1943; Macintosh, 1952); namely that the threshold to convulsive stimuli varies from person to person, in some being minimal, in others so high that even such stimuli as characterize a very severe pre-eclampsia may pass without response.

These theories do not lead to a logical basis on which to grade any given case of eclampsia. Dieckmann (1952) recommends a classification based upon the number of fits and their sequelae.

In view of the fact that the severity of the pre-existent pre-eclampsia varies greatly, it was decided to grade eclampsia, not on Dieckmann's classification, but according to the severity of the clinical signs immediately preceding the convulsions. It was thought that eclampsia supervening upon a profoundly deranged physiology would be of far graver consequence than that supervening upon a more normal state. Such a concept makes the pre-existent pre-eclampsia the denominator, and therefore infers that eclampsia is a complication of pre-eclampsia, the immediate cause of which is, at present, not known, in the sense that factors outside the simple matter of the severity of the pre-eclampsia may play important parts.

Incidence of Eclampsia

This is demonstrated in Table I. It will be seen that in the years 1938 to 1947, the rate of eclampsia in severe pre-eclampsia is very high compared to that in mild pre-eclampsia. If from these cases those are taken in which the albuminuria rose to more than 2 parts Esbach before the onset of fits, there is a 31·8 per cent risk of eclampsia (27 in 85 cases). This may be compared with a risk of 6·1 per cent (7 in 114 cases) in cases where the albuminuria did not exceed 2 parts Esbach before the appearance of the eclampsia.

From 1948 onwards, it will be seen that the overall incidence of eclampsia has decreased to

TABLE I

Incidence of Eclampsia

	In all Primigravidae		In Severe Pre-eclampsia		In Mild Pre-eclampsia	
		Per cent		Per cent		Per cent
1938–1942	21/2,669	0·8	16/86	18·6	5/352	1·4
1943–1945	14/1,814	0·8	8/53	15·1	6/279	1·8
1946–1947	14/2,060	0·7	12/60	20·0	2/730	0·3
1948–1950	12/3,182	0·4	9/174	5·2	3/550	0·6
1951–1953	8/3,183	0·3	6/216	2·8	2/527	0·4

All Booked Primigravidae, 1938–1953.

0·3 per cent (in 1952 and 1953 it was 0·2 per cent). As shown in the previous paper (Nelson, 1955) this decrease has taken place in the face of an increase in the incidence of severe pre-eclampsia. Table I shows that the fall in the overall rate is due to the improvement in the risk of eclampsia in severe pre-eclampsia. This fall coincides with the use of intensive sedation with morphine and paraldehyde in cases of severe pre-eclampsia before the onset of fits, instead of the previous practice of using the regime only after fits had occurred.

Maternal Mortality

Of all the booked primigravidae in the years 1938–1953, 12,908 in all, there was only 1 death from eclampsia or pre-eclampsia. There were 69 cases of eclampsia giving a mortality rate of 1·4 per cent. During the same period, 159 cases of eclampsia were admitted as emergencies in non-booked patients. Of these 17 died, a rate of 10·7 per cent. The rates for multigravidae and primigravidae were 16·0 per cent and 6·4 per cent respectively. Only 2 deaths occurred in 44 cases resident in the City: 4·5 per cent. The remaining 15 deaths occurred in patients resident outside the city boundaries, and for these cases the rate was 13·6 per cent. Further analysis shows that the death rate is proportionate to the distance travelled by the patient. It also increases with increasing age and parity of the patient.

Thus the low death rate of 1·4 per cent in booked primigravidae developing eclampsia compares very favourably with the rate of 6·4 per cent in unbooked primigravidae.

The value of good antenatal care backed by adequate antenatal beds is thereby demonstrated, with, in particular, the benefit of prompt and efficient treatment of the crisis when it arises, and the elimination of the necessity for the patient to travel.

The stillbirth Rate in Eclampsia

Table II demonstrates that a total of 15 infants was lost in 69 cases of eclampsia, 10 as stillbirths and 5 in the first week of life, a total rate of 21·8 per cent. In 17 patients with eclampsia superimposed upon mild pre-eclampsia, there were no baby deaths. Thus, all

TABLE II

Foetal Loss in Eclampsia

	Eclampsia occurring in:								
	Severe Pre-eclampsia			Mild Pre-eclampsia			All Grades		
	Still-birth	First Week Death	Total	Still-birth	First Week Death	Total	Still-birth	First Week Death	Total
Number	10 / 52	5 / 52	15 / 52	0 / 17	0 / 17	0 / 17	10 / 69	5 / 69	15 / 69
Per cent	19·2	9·6	28·8	0	0	0	14·5	7·3	21·8

All Booked Primigravidae, 1938–1953.

the 15 deaths occurred in the 52 cases in which the eclampsia was preceded by severe pre-eclampsia. This demonstrates that the danger of eclampsia, as far as the prognosis for the infant is concerned, is dependent mainly upon the pre-existing degree of pre-eclampsia.

Discussion

While the seriousness of eclampsia is not to be underestimated, it is important to realize that in modern clinical practice it is largely preventable by thorough sedation, and its sequelae can be modified by the promptness with which the fits are controlled; this is illustrated by the difference in the death rates in booked and emergency cases. However, it is probably wise to regard eclampsia as a disease whose importance is determined by the severity of the pre-existing pre-eclampsia. Experience shows that under good conditions, and in hospital, a fit occurring in a case of mild pre-eclampsia is probably less dangerous to both mother and child than is a severe case of pre-eclampsia uncomplicated by fits.

B. The Complications of Pre-eclampsia: Stillbirths and Neonatal Deaths

Many neonatal deaths are due to obstetrical causes, and thus resemble stillbirths. The term "perinatal" deaths has been used to include all such deaths. Duncan, Baird and Thomson (1952) have coined the term "obstetric death" to signify stillbirths and all first week deaths, on the grounds that it will include practically all deaths due to the processes of pregnancy and labour. In the analyses which follow, the first week death rate is given as deaths per 1,000 total births and not per 1,000 live births, so that a straight addition can be made between stillbirths and first week death rates to give the total, or obstetric death rate.

Association of Pre-eclampsia and Deformity

The incidence of deformities incompatible with life in this series is 20 cases in a total of 3,027 pre-eclamptic pregnancies. This is a rate of 7 per 1,000. Three cases occurred in 589 severe pre-eclamptic pregnancies—5 per 1,000; and 17 in 2,438 mild pre-eclamptic pregnancies —7 per 1,000. Thus, the incidence of deformity incompatible with life in pre-eclampsia is a little less than it is in the general population. It may be inferred, therefore, that there is no significant relationship between deformity and pre-eclampsia.

Overall Obstetric Death Rates in Pre-eclampsia

In severe pre-eclampsia, the stillbirth rate was 71, the first week death rate 42, giving a total rate of 113. These figures are calculated from the whole series, 1938–1953.

In mild pre-eclampsia, the stillbirth rate was 22, the first week death rate 7, giving a total rate of 29. These figures are calculated on the booked married City primigravidae, 1948–1953, for reasons outlined in the previous paper (Nelson, 1955).

These rates illustrate that the presence of albuminuria signifies a much greater risk to the foetus, a fact which has long been recognized and accepted. The obstetric death rate, however, in mild pre-eclampsia is less than that for all primigravidae from all causes (38)*. This confirms the impression that mild pre-eclampsia has, in fact, little or no adverse effect upon the baby.

The Effect of Age upon the Outcome for the Foetus

The Table III shows the obstetric death rates in severe pre-eclampsia, analyzed by age. In the age group 20–24, the rate is about double that for all causes in the general primigravid population in the same age group. This relationship persists into the 25–29 age group, but over the age of 30 the rate increases much faster in severe pre-eclampsia than in the general primigravid population; in the 30–34 age group the rate in severe pre-eclamptics is almost 4 times that in all primigravidae, and in the age group 35-and-over exactly 4 times greater. The rise in the obstetric death rate is entirely due to a rise in the stillbirth rate, which fact emphasizes the increased risk of intra-uterine death in the older primigravidae with pre-eclampsia.

Another striking, if rather unexplained, feature is the high obstetric death rate in the 19-and-under age group. This high rate is probably not the effect of extreme youth so much as a result of the fact that many women in this group are of poor physique and live under slum conditions. (See next section.)

The total obstetric death rate of 113 in severe pre-eclampsia is almost 3 times that of the primigravid population; this is largely due to the great increase in the rate over the age of 30, and to a lesser extent to the increased rate under the age of 20.

Table IV shows that there is no comparable effect of age upon the obstetric death rates in mild pre-eclampsia. Were mild pre-eclampsia a true mild version of the severe grade, one would expect that the obstetric death rates would be influenced in a similar fashion, though to a lesser degree. This may be taken as further evidence to that put forward previously (Nelson, 1955) that mild and severe pre-eclampsia are not necessarily the same disease process.

* This figure refers to all booked primigravidae, 1948–1953.

TABLE III

A.—Obstetric Deaths in Association with Severe Pre-eclampsia

All Booked Primigravidae, 1938–1953 (includes Eclampsia graded according to pre-existent Pre-eclampsia)

	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Stillbirths	7/76	92	7/264	27	11/169	65	10/56	179	7/24	290	42/589	71
First Week Deaths	5/76	66	10/264	38	6/169	36	3/56	54	1/24	42	25/589	42
Obstetric Deaths	12/76	158	17/264	65	17/169	101	13/56	233	8/24	332	67/589	113

B.—Obstetric Deaths in all Booked Primigravidae, 1938–1953 from all causes

	Under 20	20–24	25–29	30–34	35+	All Ages
Obstetric Death Rate	37	34	47	63	86	42

The Effect of Social Class upon the Outcome for the Foetus

The years 1948–1953 are used to assess this factor, for reliable social class data is available only for this period, in the cases married and resident in the City of Aberdeen. As it has been shown that mild pre-eclampsia has little or no effect upon the prognosis for the foetus, only the obstetric deaths in association with severe pre-eclampsia will be examined. Furthermore, as mentioned above, figures cannot be augmented by adding mild and severe pre-eclamptic cases together. Unfortunately this limits the figures now available for study, and they are too small to allow of reliable conclusions being drawn; nevertheless, the findings are of definite interest.

Table V shows that the obstetric death rate is lowest in Social Classes I and II despite the fact that about 30 per cent of the patients were over the age of 30; the rate is highest in Social Classes IV and V where only about 10 per cent of the patients were over the age of 30. The highest rates were in Social Classes III, IV and V over the age of 30, and Social Classes IV and V under the age of 20.

Obviously, no firm conclusions can be drawn

TABLE IV

Obstetric Deaths in Association with Mild Pre-eclampsia

	Under 20		20–24		25–29		30–34		35+		All Ages	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Stillbirths	5/86	35	7/421	17	3/202	15	2/94	22	2/47	43	19/849	22
First Week Deaths	0/86	0	3/421	7	3/202	15	0/94	0	0/47	0	6/849	7
Obstetric Deaths	5/86	35	10/421	24	6/202	30	2/94	22	2/47	43	25/849	29

Booked Married City Primigravidae, 1948–1953. (Includes Eclampsia graded according to pre-existent Pre-eclampsia.)

TABLE V

Obstetric Death Rates in Severe Pre-eclampsia by Social Class

Social Class	Under 20		20–24		25–29		30+		All Ages	
I and II	0/2	0	0/5	0	3/16	188	0/11	0	3/34	88
III	1/23	44	5/111	45	5/71	78	5/19	263	16/224	102
IV and V	2/14	142	3/41	72	0/12	0	4/8	500	9/75	120
All Classes	3/39	77	8/157	51	8/99	80	9/38	237	28/333	84

Booked Married City Primigravidae, 1948–1953. (Includes Eclampsia graded according to pre-existent Pre-eclampsia.)

TABLE VI

Height and Obstetric Deaths in Severe Pre-eclampsia

	Under 20 No.	Under 20 Rate	20–24 No.	20–24 Rate	25–29 No.	25–29 Rate	30+ No.	30+ Rate	All Ages No.	All Ages Rate
Tall: 5 feet 4 inches+	0/5	0	5/44	114	3/31	97	4/14	286	12/96	125
Medium: 5 feet 1 inch–5 feet 3¾ inches	3/25	120	6/106	57	2/62	32	5/24	208	16/217	74
Small: Under 5 feet 1 inch	4/42	95	3/57	53	6/31	194	4/12	333	17/216	79

All Booked Primigravidae, 1944–1947.
Booked Married City Primigravidae, 1948–1953.

from these figures, but they do suggest that two factors which influence the obstetric death rate in severe pre-eclampsia are increasing age and poor social status. Conversely, in young healthy women the rate is correspondingly low. It was shown previously (Nelson, 1955) that social status and age had little effect upon the incidence of severe pre-eclampsia; but this analysis suggests that they do, in fact, have a profound influence upon the outcome for the foetus in severe pre-eclamptic pregnancies.

The Effect of Maternal Height upon the Outcome for the Foetus

For reasons given previously (Nelson, 1955), height may be used as a substitute for social class in that stature is influenced to a great extent by the conditions and diet obtaining in the woman's years of growth. For this reason the effect of maternal height on the obstetric death rate in severe pre-eclampsia has been studied as a check upon the findings in the social class analysis. To the cases analyzed in Table V have been added those for the years 1944–1947, for height was routinely measured from 1944 onwards. There is no satisfactory evidence for a height effect operating consistently throughout individual age groups. The overall obstetric death rate is higher in tall women, probably because there are relatively more tall women over the age of 30 years than in the other two height groups.

The Decline in Obstetric Death Rates in Severe Pre-eclampsia since 1938

In the assessment of factors which influence the obstetric death rate in any given population, it is a matter of the greatest importance that a frame of reference is given for the present figures. The truth of this can readily be seen from Table VII in which the changes in the obstetric death rate during the past 16 years are set out.

It will be seen that there is a steady decline in the obstetric death rate throughout the period reviewed, and that this is dependent entirely upon a steady fall in the stillbirth rate. In the year 1953, of 67 cases of severe pre-eclampsia there were no stillbirths, and only 3 first week deaths, 1 of which was a deformity (cardiac malformation). Figure 1 shows graphically the very striking and steady fall in the stillbirth rate, and the much less constant progress of the first week death rate (the very low figure for the latter in 1943–1945 cannot be explained on grounds other than chance variation).

No certain explanation can be given for these changes, but certain possibilities may be mentioned.

Firstly, the general all-round improvement in the standards of both antenatal care and the care of the newborn. During the period under review the proportion of primigravidae in the city confined in hospital has risen from 25 per cent to 85 per cent. Early admission to hospital

TABLE VII

A.—Obstetric Death Rates in Severe Pre-eclampsia, 1938–1953

All Booked Primigravidae: Cases of Eclampsia Occurring in Severe Pre-eclampsia Included

	Whole Series									
	1938–1942		1943–1945		1946–1947		1948–1950		1951–1953	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Stillbirths	13/86	151	6/53	113	5/60	83	12/174	69	6/216	28
First Week Deaths	5/86	58	1/53	19	3/60	50	7/174	40	9/216	42
Obstetric Deaths ..	18/86	209	7/53	132	8/60	133	19/174	109	15/216	70

B.—1948–1953 in Detail

	1948		1949		1950		1951		1952		1953	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Stillbirths	4/60	67	4/52	77	4/62	65	3/81	37	3/68	44	0/67	0
First Week Deaths	4/60	67	2/52	38	1/62	16	3/81	37	3/68	44	3/67	45
Obstetric Deaths ..	8/60	134	6/52	115	5/62	81	6/81	74	6/68	88	3/67	45

for assessment, of all cases showing early signs of pre-eclampsia and the treatment with adequate and intensive sedation of the established severe pre-eclamptic has gradually become accepted policy. Of 890 booked married City primigravidae in 1953, 143 (16·0 per cent) spent an average of 7·4 days in the antenatal wards under treatment for pre-eclampsia of all grades. Caesarean section, however, has not been used to any extent (3·5 per cent of cases of severe pre-eclampsia since 1948), and pre-eclampsia was seldom the only indication.

Secondly, the broad general factor that the stillbirth rate from all causes has fallen very strikingly during the same period. Evidence has been produced by Baird, Thomson and Duncan (1953) that this fall in the stillbirth and first week death rates (most marked during the war), especially from prematurity, was very much aided by full employment and the government's war-time food policy. The present figures for pre-eclampsia—showing a tendency to high rates in Social Classes IV and V, both old and very young—suggest that any further improvement in living standards for this group would have a favourable effect upon the overall obstetric death rate in severe pre-eclampsia.

Many influences, therefore, are at work besides the actual disease in question, influencing the foetal survival rate. Probably age and the factors implicit in social class—physique, diet, environment—are almost as important as the

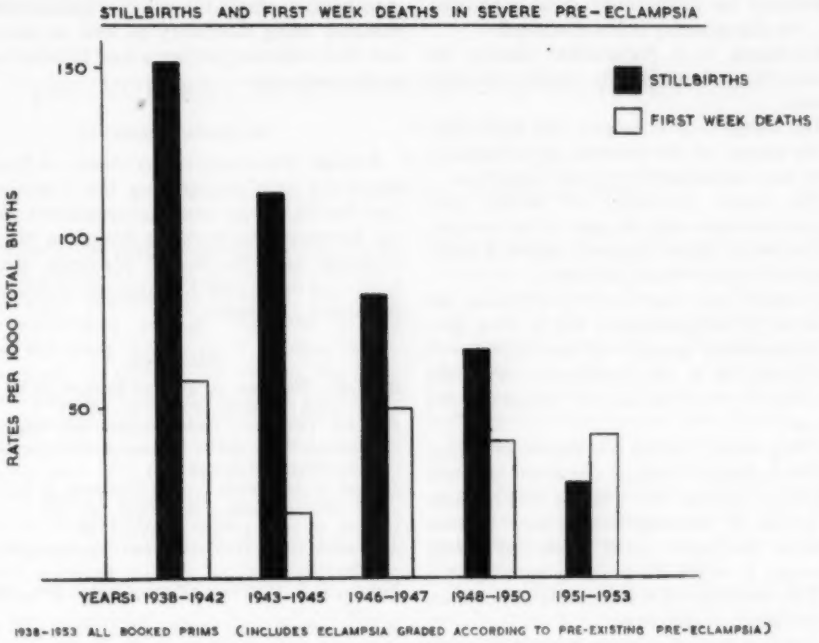

FIG. 1

severity of the pre-eclampsia and the mode of treatment.

SUMMARY AND CONCLUSIONS

The danger of eclamptic seizures is determined by the severity of the pre-existent pre-eclampsia, and by the standard of treatment the patient has received up to the time of the convulsions. Consequently, maternal and foetal mortality will vary greatly according to circumstances. With the best available standards of obstetrical care the incidence of eclampsia in primigravidae in Aberdeen is now 0·2 per cent (1952 and 1953). No death has occurred since 1942 from eclampsia in a booked primigravida. Taking the whole 16 years, there were 69 cases of eclampsia in 12,908 primigravidae with only 1 death.

In 589 cases of severe pre-eclampsia (1938–1953) and 849 (1948–1953 only) cases of mild pre-eclampsia, obstetric death rates of 113 and 29 respectively were found. While the eclampsia and obstetric death rates have fallen, the actual incidence of severe pre-eclampsia has risen (see previous publication, Nelson, 1955).

The prognosis for the foetus is unlikely to be improved any further by present lines of treatment. Any further fall in the obstetric death rate is likely to be due to a decrease in the proportion of primigravidae over 30, or an improvement in the physique, health, and living conditions of those in the lower income groups. Conversely, the rate may rise with any reverse trends towards increasing age and poor standards of living.

Together with the previous publication, this epidemiological investigation of pre-eclampsia and its main complications has shown that:

(1) The incidence of pre-eclampsia is equal throughout the social class range as it is at present constituted.

(2) The incidence of pre-eclampsia has not

been lessened by increasingly strict standards of care; on the contrary it has increased.

(3) Eclampsia is a preventable disease, its incidence being lessened by good obstetric standards.

(4) The dangers of eclampsia are dependent upon the degree of pre-existing pre-eclampsia; and they can be mitigated by good obstetrics.

(5) The foetal mortality in severe pre-eclampsia increases with the age of the mother, and as her social status decreases, and is difficult to mitigate by good obstetrics alone.

This enquiry has done little to elucidate the basic cause of pre-eclampsia, but it does give a well documented account of the incidence of the condition in a city population, and the progress made in minimizing the dangers of the condition.

It is often stated, but on incomplete evidence, that pre-eclampsia is more common in some areas than in others. The truth of this remains to be tested. If investigations similar to that reported in this paper could be carried out in other areas, it might be possible to settle the point. This would be of considerable importance from the aspect of aetiology.

As an addendum, it may be claimed that this investigation shows the value of epidemiological research using morbidity as well as mortality, and that obstetric problems lend themselves well to this technique.

Acknowledgments

I would like to record my thanks to Professor Baird for help in initiating this investigation, and for his advice and encouragement; also to the Secretarial Staffs of the Aberdeen Maternity Hospital and the Social Medicine Research Unit attached to the Department of Midwifery, Aberdeen University.

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THE NURSERY REQUIREMENTS OF *XENOPUS LAEVIS*

BY

I. M. LARKIN, B.Sc., B.S., M.D.

Portsmouth and Isle of Wight Pathological Service

THE demand for early pregnancy diagnosis by means of biological assay of urinary chorionic gonadotropin continues to increase. The most firmly established test is undoubtedly the Hogben test using the female of *Xenopus laevis*.

This toad is difficult to obtain in large numbers and costly to import from abroad. It also has the reputation of being difficult to breed. This reputation is in fact quite undeserved. By the application of a few lessons gained from a study of their natural history, prolific reproduction is readily accomplished.

Although large Hogben Units may be costly to install, a colony suitable for the usual requirements of a general hospital laboratory can easily be maintained, using inexpensive mass-produced aquarium equipment. Anyone contemplating setting-up a Hogben Unit cannot do better than consult the admirable and comprehensive account of B. M. Hobson (1952). The crux of the matter is to contrive a constant temperature and at the same time water running at a sufficiently modest rate to occasion a complete change of water in each tank in every 24 hours.

The main problem, therefore, is the acquisition of toads. The following is an account of the rearing of some 600 toads from eggs last season on a roof in the centre of Portsmouth. These were the offspring, at a single spawning, of two pairs of toads. The "infant mortality" was practically nil.

PRODUCING FERTILE EGGS

The constant temperature, monotonous diet, unnatural environment, exclusively female society and lack of sunshine are probably all factors which conveniently conspire to prevent spontaneous oviposition in the laboratory.

Bearing this in mind, early in the New Year, 1953, 6 female toads (all known reactors) were withdrawn from the test tanks and 6 males were set aside with them. They were put in glass tanks with water weed and given live food and varied diet whenever possible. Chopped worms are admirable. As the season advanced, they were taken on to the flat roof of the laboratory building whenever the sun was shining.

When the weather became quite warm early in June, about 60° F. in the shade, 2 pairs were segregated in separate tanks and left permanently on the roof. They were supplied with "pond" water and water-weeds and left to themselves. They spawned after a few days.

The remaining 4 pairs were packed in tins and sent by train to Essex to act as "reserves". They were turned loose in a privately owned pond and spawned repeatedly throughout the summer, producing many thousands of tadpoles. These would have been netted and returned to Portsmouth if needed, but the occasion did not arise.

It should be remarked at this point that it is possible to induce the male toad to produce spermatozoa at will, and the female to produce ova, by injecting gonadotrophic hormone. This is not by any means the same thing as achieving fertilization and experience has shown this method of approach to be a failure.

To return to the glass tanks on the Portsmouth roof. The pairs of toads were removed as soon as spawning was accomplished, and the young tadpoles hatched out at the end of a week.

REARING THE TADPOLES

It was anticipated that (like the young of English frogs) the tadpoles would probably be vegetarian at first and later develop a taste for "meat". A convenient sweet and matured pond was located, and water was taken from it every few days, together with a good supply of the

common pond-weeds. Pond water and weeds were added to the tadpole tanks every day. When first put in, it was green with innumerable microscopic organisms, like Volvox, Chlamydomonas, Euglena, etc., but after a few hours the tadpoles invariably "cleared" the water. From this it was judged that they must, at any rate in part, be filter feeders. Further weight was given to this notion when it was observed that they make mouth-and-pharynx respiratory movements, passing a constant stream of water over gills which are hidden beneath an operculum.

Metamorphosis

In this way the tadpoles continued to thrive and grow. Fig. 1 shows the appearance at about 2 weeks, Fig. 2 at about 6 weeks, Fig. 3 at about 8 weeks. The hind legs appear first, then the fore-limbs. The tail very rapidly withers and disappears and then the whole animal appears to shrink (due probably to atrophy of the gills) and becomes a tiny toad (Fig. 4). In the later

Fig. 1
Xenopus laevis tadpole. About 2 weeks. ×2.

Fig. 2
Xenopus laevis tadpole. About 6 weeks. ×2.

Fig. 3
Xenopus laevis tadpole. About 8 weeks. ×2.

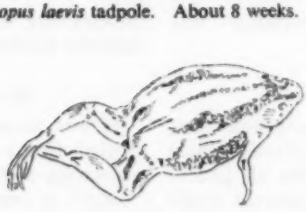

Fig. 4
Xenopus laevis. Later stage. ×2.

stages the little animals can be seen to come to the surface from time to time to take a minute gulp of air. In most cases the process of metamorphosis took about a fortnight.

This phase was obviously a critical one, and live Daphnia were introduced into the tanks. They were greatly appreciated by the late tadpoles and young toads and consumption was at the rate of thousands per day. (However, they can be obtained from the local pet-shop for 6d.)

At the same time it was borne in mind that metamorphosis is dependent upon a properly functioning thyroid gland which probably "works overtime" during this event. It was reasoned that in the densely populated tanks, iodine deficiency was a real danger. An arbitrary amount of 20 drops of a saturated solution of K.I. per gallon of water was added twice per week to each tank.

Rearing the Toads

The diet of our adult toads is frozen condemned ox liver which is supplied weekly at moderate cost by a local slaughterhouse. It was therefore desirable to get the young toads on to a liver diet as soon as possible. If we had added finely chopped liver to the tadpole tanks, the unconsumed residue and "juice" would have putrified in a few days. It was impracticable to change the water and clean out the tanks daily in the presence of so many hundreds of small delicate animals—some air-breathing and some water-respiring.

At this stage we were presented with two full-size house-baths from a part of the hospital undergoing demolition. These were taken up to the roof and fixed up so that water ran in constantly at one end at a temperature of 60 to 70° F. and out through an overflow pipe with a small gauge wire filter at the other end. The rate of flow in each bath was about 1 pint every 3 minutes.

The young toads were divided evenly between the two baths and gradually weaned from live Daphnia to daily finely chopped liver. A little cod-liver oil was added once a week mixed with the liver. Water weed was grown freely in the baths. In this way the water kept sweet and clear and the baths only needed very occasional cleaning.

The growing toads fed voraciously and as they increased in size the liver was chopped less finely. They soon learned where to congregate at feeding time.

As the weather grew colder, the baths were packed round with sacks of straw and covered over at night. The inflow of pre-heated water in these circumstances has sufficed to keep the baths at from 50 to 65° F. even on the coldest nights and the toads have maintained the greatest possible activity and appetite. By the end of November many of them had reached a weight of 70 grammes (our minimum standard of size for test animals) and at the present time (middle of January) well over half are a good deal more than this. In a few weeks we shall be sexing the new stock and testing the females for sensitivity with a dose of 70 I.U. of C.G. (Hobson, 1952). In a little while longer we should have substantial reinforcements for our hard-pressed and ageing original colony.

Summary

The demand for Hogben tests continues. Small colonies can easily be maintained at little cost by means of "hobby" aquarium thermostatic equipment. *Xenopus* toads are difficult to come by except in small numbers, but reproduction is prolific and easily accomplished if a few simple rules are followed.

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EARLY ECTOPIC PREGNANCY

Comments on Conservative Treatment

BY

JØRGEN LUND, M.D.

From the Surgical Department A of the Gentofte County Hospital
Chief: Professor Poul Morville, M.D.

THE treatment of extra-uterine pregnancy presents no great problem to most surgeons and gynaecologists; operation is the method of choice everywhere as soon as the diagnosis has been established. Acute forms of ectopic pregnancy should be operated on at once; there is no room for discussion here, because the bleeding has to be arrested. But it is still doubtful whether operation should be performed in all cases in which the disease—as is often seen—occurs without alarming symptoms of internal haemorrhage.

As is known, follow-up studies of patients who have been previously operated on for ectopic gestation show that a high proportion have become secondarily sterile. It would be of very great importance if methods of treatment could be elaborated which would diminish the frequency of this secondary sterility without other disadvantages. The question is, therefore, whether the ordinary therapy should be abandoned in suitable cases in order to increase future fertility. The present investigation was designed to elucidate whether conservative—non-surgical—treatment of ectopic pregnancy (which is known to be localized in about 98 per cent of cases to the Fallopian tube) leaves the tubes capable of reproduction.

Most clinicians have observed that ectopic gestation may terminate spontaneously without any alarming symptoms; verified cases have repeatedly been reported in the literature (e.g., Borell, 1921; Cox and Steinberg, 1942; François and Isidor, 1934; Leith Murray, 1932; Schumann 1926). But no investigations have been published on systemic experiments with non-surgical treatment.

At the time when Lawson Tait (1884) of Birmingham, almost 70 years ago, introduced the operative treatment of extra-uterine gestation with acute haemoperitoneum the disease was considered very serious; the mortality was stated to be as high as almost 70 per cent (Parry, 1876). The cause of this was that ectopic pregnancy could not then be diagnosed until a catastrophe had occurred; if the course of the disease was more quiet, it was not recognized. The dramatic decrease in mortality following the introduction of the surgical treatment was most impressive to Lawson Tait's contemporaries. It was, therefore, quite natural that, as the subacute types of the disease became universally known a few years later (Veit, 1884, 1886; Werth, 1887), these forms were also subjected to operation. During the last fifty years or so it has thus been the method of choice almost everywhere to operate on every early ectopic pregnancy, irrespective of the amount of blood-loss. Consequently, we know nothing definite about the risk of consistently avoiding operation in the subacute forms of the disease.

It is not possible to establish on a rational basis the indications for operation before the following questions have been answered:

(1) What is the clinical course of early subacute ectopic gestation when the patient is not operated on?

(2) What do follow-up examinations of such cases show with regard to fertility?

The present investigation was made in order to contribute to the solution of these two problems.

AUTHOR'S MATERIAL

In the course of the years 1930–46 inclusive, 381 cases of ectopic pregnancy were treated in

the 3 surgical departments (A, D and H) of a Copenhagen hospital (the Gentofte County Hospital). In the two departments (A and D) conservative treatment of the subacute cases was attempted (termed Group I), whereas in the third department (H) operative treatment was used as a routine method in dealing with all patients with extra-uterine pregnancy, including subacute cases (termed Group II). The cases are distributed as shown in Table I.

TABLE I

Author's Material

	All Cases	Subacute Cases
Departments A and D ..	215	119 (Group I)
Department H	166	85 (Group II)
Total	381	204

The series of cases analyzed in the present paper consists of Groups I and II which have been treated differently (see text) and in which the results of treatment have been compared. The subacute cases include all patients who had no demonstrable haemoperitoneum on admission and were not acutely ill.

Group I. Almost half the number of the 215 patients with ectopic pregnancy admitted to departments A and D displayed signs of a large intraperitoneal haemorrhage ("catastrophe"); these patients were treated by immediate operation (if indicated, after transfusion). The rest of the patients, 119 cases (i.e., 55 per cent), were not acutely distressed on admission; conservative treatment was attempted in all these cases. This is Group I. These 119 cases only include patients with a typical course of the disease and with positive pregnancy tests (Aschheim-Zondek and, later, Friedman's test). Therefore the diagnosis is practically certain, even though it has not been verified by operation. It is very rare to find any other disease with the same clinical course as an ectopic pregnancy and a simultaneously positive pregnancy test (certain corpus luteum cysts, see Heiberg, 1939; Israel, 1942; Te Linde and Henriksen, 1940; Gordon Luker, 1921).

Group II. The case records of the 166 patients of the department H where, as already mentioned, *all* cases with ectopic pregnancy were consistently subjected to operation, have been studied closely. According to the condition of the patients on admission such cases have been selected as did not show signs of haemoperitoneum ("catastrophe"), i.e., patients which would have been given a conservative treatment according to the criteria mentioned above. This gives Group II comprising 85 cases (see Table I); the table shows that both groups (Group I and II) represent a little more than 50 per cent of the total series of ectopic pregnancy in these departments. In other series a similar distribution has been found between acute and subacute forms (Atlee, 1947; Dodds, 1940; Holtz, 1936; Leith Murray, 1932; and others). No tendency has thus been found to press patients into the group of subacute cases, which might well be possible in departments where conservative treatment is used.

It will be noticed that Groups I and II are composed of the same types of the disease, that they have been treated in the same hospital and, therefore, originate from the same population; lastly they have been dealt with during the same period of time (1930–1946). The only difference between the groups is in the treatment, and this alone can, therefore, have determined possible differences between the groups found in the follow-up studies.

CONSERVATIVE TREATMENT OF ECTOPIC PREGNANCY

The treatment consisted in confinement to bed with close observation during the first few days when constipation was encouraged by means of opium. Pregnancy tests were made at intervals of from 7 to 10 days, and vaginal examinations were regularly made. Gradually a more liberal regime was instituted according to the patients' condition. Patients were not allowed out of bed until the Friedman test was negative and the pain had ceased. Table II shows that this non-operative treatment could be carried through in only 68 out of 119 cases, i.e., in 57 per cent.

It was found that by means of this regime upwards of half the number of the patients were freed from pain within the first week after admission. The rest had intermittent pain for a prolonged period. As shown in Table II the con-

TABLE II

Immediate Results of Attempts at Conservative Treatment in 119 Cases (Group I)

No operation	68 cases
Operated on owing to "catastrophe" ..	27 cases
Operated on for other reasons	24 cases

The Table shows that non-surgical treatment could be effected in only 68 out of 119 cases, i.e., 57 per cent.

servative treatment had to be discontinued in many cases. Operation was of course performed at once in case of signs of a large, intra-abdominal haemorrhage. But it was attempted to avoid operation when there were only slight signs of internal bleeding (without appreciable anaemia). Finally, operation was undertaken in the case of patients who did not, after 3–4 weeks stay in hospital, show signs of the disease becoming quiescent (i.e., when the Friedman test remained positive and the adnexal swelling was still tender).

In the 68 cases not subjected to operation (Table II) the Friedman test changed from positive to negative in the course of the first 3 to 4 weeks in hospital. If expectant treatment had been continued for a longer period, it is likely that a still greater number of tests would have become negative. The limit of 3 to 4 weeks mentioned has, however, been fixed as a reasonable time within which the reaction might be expected to change. In ectopic pregnancy there has thus been shown a tendency to spontaneous cessation of the trophoblastic activity (followed by resorption of the ovum).

The risk in the conservative treatment of ectopic pregnancy is the ever-present possibility of large, intra-abdominal haemorrhage—"catastrophe". This occurred in the course of conservative treatment in 27 patients (Table II), and in many cases the catastrophe occurred quite suddenly in a painless period without warning (such as increased abdominal tenderness or anaemia). In 25 out of the 27 cases, vaginal examination a few days before the acute symptoms began had revealed a very tender or increasing swelling. These findings in a patient with ectopic pregnancy may thus suggest continued trophoblastic activity. In the present series, experience has shown that bimanual examination provides the most reliable information about the patient's condition. If the swelling subsides and the tenderness decreases, the risk of a large haemorrhage is passing, whereas cases with a persistently tender or increasing mass are still in danger. It may here be mentioned that many patients in the group of 24 (Table II) were operated on because of increasing or persistent tender swelling (but without acute symptoms). In most of these cases (15 out of 19) fresh haemorrhage was found around the ovum at operation.

There is some disagreement among gynaecologists as to the importance of the Friedman test as a guide in the treatment of ectopic gestation. Some consider that a negative pregnancy test will preclude catastrophe, whereas others maintain that this may occur despite a negative test (Farell and Scheffey, 1943; Schauffler and Wynia, 1941). It is well established that in ectopic gestation there is close correlation between the degree of degeneration of the chorionic villi and the results of the pregnancy tests (see Goldblatt and Schwartz, 1940). If this correlation holds good in all cases, it will be difficult to imagine what is the pathological basis of the development of a catastrophe in cases with a negative Friedman test. One of the patients in the group of 27 (Table II) had a negative pregnancy test at the time when she was operated on (tubal abortion with large haemorrhage); the reaction was positive in the other patients in this group. Among the remaining 24 cases operated on (Table II) 16 had a positive pregnancy test at the time when they were operated on—all 16 cases had well preserved chorionic villi. Eight patients were operated on when the test was negative. In 7 of these there were no fresh haemorrhages while the eighth case showed well preserved chorionic villi and a small fresh peritubal bleeding. Finally it may be mentioned that no large haemorrhage occurred after the pregnancy test had become negative in any patient of the 68 who were not operated on.

It thus appears that in case of a negative Friedman test the risk of catastrophe is slight. But like any other biological test the Friedman reaction is not absolutely reliable. A negative result does not entirely preclude continued

trophoblastic activity. Only when both the Friedman test and the clinical examination show that the disease has become quiescent, can we be fully convinced that the risk of catastrophe has passed. To illustrate this it may be mentioned that the 2 patients who had a fresh haemorrhage in spite of a negative pregnancy test both had considerable, tender pelvic swellings.

The immediate results of conservative treatment are shown in Table II. The group of 24 cases operated on comprises 19 patients in whom laparotomy was performed owing to a persistently growing swelling and 5 in whom the pregnancy test remained positive. Conservative treatment was thus successfully carried out in less than one-third of all 215 cases admitted (Table I). One death occurred in Group I; a patient with an increasing pelvic mass was operated on and tubal pregnancy and tuberculous salpingitis were found. The patient died of miliary tuberculosis 4 months later. The method cannot be blamed for this case.

Nothing suggested that the age of pregnancy (as far as this can be given) exerted any influence on the chance of carrying through non-operative therapy (Table III).

TABLE III

Age of Pregnancy and Frequency of Operation

Age of Pregnancy	Number of Cases	Operated on
Under 6 weeks	44	18 (41%)
More than 6 weeks	71	31 (43%)

The age of the pregnancy is given as the time interval between the last normal menstruation and the date of admission. There is no difference in the frequency of operation between the two groups.

The stay in hospital of some of the patients during conservative treatment was rather prolonged; 60 per cent of the cases were hospitalized for more than one month (Table IV). In Group II (Table I), which consists of 85 patients who were operated on, the stay in hospital was generally shorter than in Group I (Table IV). Sixty per cent of Group II were in hospital less than one month.

One death occurred in Group II (post-operative intestinal obstruction). Another patient of this group developed post-operative obstruction but recovered after further operation.

TABLE IV

Duration of the Stay in Hospital in Groups I and II
Percentage figures

Duration of Stay in Hospital	Group I	Group II
10–20 days	19	14
20–30 days	21	47
30–40 days	30	22
40–50 days	14	11
Over 50 days	16	6

The duration of the stay in hospital is longer in Group I. It may be mentioned that many of the patients in Group II were operated on before the introduction of early mobilization (and discharge) after operation.

It appears that the conservative treatment employed here has no higher mortality than the operative therapy. But the conservative management has a number of drawbacks:

(1) The treatment can only be carried through in about one-third of all ectopic pregnancies.

(2) A certain number of patients get a large, intraperitoneal haemorrhage which could have been prevented by early operation.

(3) The patients have to stay longer in hospital than in operative treatment.

FERTILITY AND ECTOPIC PREGNANCY

As mentioned in the introduction, it is the general view that the fertility of women with ectopic pregnancy is decreased, especially after the disease. There is some controversy regarding the question whether the premorbid fertility is lowered (Beacham *et al.*, 1948; Farell and Scheffey, 1943; Fitzgerald and Brewer, 1935; Lisa *et al.*, 1942; Masson, 1930). In the cases examined by the author the number of children per patient before the disease has been calculated as far as the 180 married patients are concerned. The patients were divided into age-groups and the number of children was compared with that of children per married woman in the population of Copenhagen. The results are shown in Table V. It seems clear that the premorbid fertility (i.e., the *matrimonial* fertility) in ectopic pregnancy is not lowered.

TABLE V

Premorbid Fertility in Ectopic Pregnancy

Age	Number of Patients	Number of Children	Children per Patient	Children per Married Woman in Copenhagen
Years				
20–24	17	9	0·53	0·64
25–29	58	55	0·95	0·91
30–34	61	69	1·13	1·18

The Table shows that there is no significant difference between the number of children in patients with ectopic pregnancy and in the population from which the patients originate.

Recent large series distinctly show a considerably reduced frequency of conception after the disease (Apajalahti, 1932; Berg, 1936; Haffner, 1940; Holtz, 1936; Malice, 1926; Masson and Simon, 1927; Mayo and Strassmann, 1938; Schneider, 1934; Sserebroff, 1932; Wenig, 1927). In the follow-up examinations by the authors just mentioned it has most frequently been found that about 40 per cent of the patients operated on later conceive. This percentage refers only to the patients who are not anatomically sterile after the operation. The point of importance is, of course, to know how many of all the patients treated (operated on) conceive. This can be calculated from some of the statistics published; the figures vary from 20 to 30 per cent. These percentages show some variation according to the length of the period of observation, but they distinctly show that a relatively small proportion of patients have children later.

RESULTS OF THE FOLLOW-UP

The follow-up of the patients in Group I showed that over 40 per cent have later had one or more intra-uterine pregnancies. Though this is more than the 20 to 30 per cent mentioned above, it does not justify the conclusion that the conservative treatment increases the patient's chances of subsequent pregnancy. Owing to a number of differences between the series considered (first and foremost with regard to the duration of the periods of observation and the percentage of cases followed up) a direct comparison with the present series of cases is not possible.

In Groups I and II the 119 and the 85 cases represent 113 and 84 patients respectively. The number of patients is given in Table VI. In both groups were 75 per cent followed up for 5 years or more. The remaining cases have been followed for a period between 3 and 5 years.

TABLE VI

Series of Cases Followed up

	Number of Cases	Number of Patients	Deaths	Series	Followed up
Group I	119	113	1	112	108 (96%)
Group II	85	84	1	83	79 (95%)

The percentage of patients followed up is the same in both groups.

The results of the follow-up are shown in Table VII. It may be mentioned that one patient has had both an ectopic pregnancy subjected to conservative treatment (included in Group I) and a tubal pregnancy dealt with by operation (included in Group II). This patient has to be left out of both groups when they are to be compared (therefore the number of cases followed up is 1 less in each group in Table VII than in Table VI).

TABLE VII

Results of Follow-up

	Group I	Group II
Number of patients followed up	107	78
Wanted children (i.e., contraceptives not used)	101	73
Intra-uterine pregnancies ..	46 (46%)	32 (44%)
Extra-uterine pregnancies ..	15 (15%)	11 (15%)

The Table shows no significant differences between the number of intra-uterine and extra-uterine pregnancies respectively in the two groups.

The average number of pregnancies per patient in both groups is given in Table VIII.

It appears from Tables VII and VIII that no differences in postmorbid fertility were demonstrated between Groups I and II. That these

TABLE VIII

Number of Pregnancies per Patient

	Group I	Group II
Patients wanting pregnancy ..	101	73
Total number of deliveries ..	64	48
Total number of abortions ..	14	9
Total number of intra-uterine pregnancies	78	57
Pregnancies per patient	0·8	0·8

There is no difference between Group I and Group II.

two groups are directly comparable appears from the following: they comprise the same types of the disease; they are distributed alike with regard to the period of observation and age; they are treated in the same period, and, finally, they have been followed up to the same extent (95 per cent). According to this conservative treatment has clearly not resulted in a greater fertility than that seen after operation. Broadly speaking, the Fallopian tube that has been the site of ectopic pregnancy is useless as an organ of reproduction. Presumably however it cannot be considered quite out of question that a tube previously diseased in this manner may not again become permeable. The 11 patients of the present series shown in Table IX are interesting in this respect. Apparently the risk of a renewed ectopic pregnancy is greater than the chance of intra-uterine pregnancy.

TABLE IX

	Pregnancies	
	Intra-uterine	Extra-uterine
9 patients with previously unilateral salpingectomy; later, conservative treatment of ectopic pregnancy ..	0	2
2 patients with two contralateral ectopic pregnancies, subjected to conservative treatment	1	0

At the follow-up of these 11 patients (author's series), all of whom wanted pregnancy, it appeared that only 1 had had an intra-uterine pregnancy.

Hysterosalpingography was performed at the follow-up examination in about half the patients subjected to conservative treatment. In almost all the cases marked changes were found as a rule with tubal occlusion. A number of patients had hydrosalpinges; a few displayed the typical picture of endometriosis localized to the isthmus of the tube (see Bertelsen, 1943; Madsen, 1943). A few other patients with an identical picture of isthmical endometriosis were previously operated on. The operation specimens displayed pregnancy in the ampulla of the tube and no tubal endometriosis. These findings are presumably analogous with the "postsalpingectomy endometriosis" previously described by Sampson (1930) as found in tubal remnants in salpingectomized patients.

CONCLUSIONS

(1) It is shown that conservative treatment of subacute ectopic pregnancy does not involve greater risks than operation. Conservative treatment requires close supervision, is of rather long duration and can only be carried out in upwards of half the number of the cases. The rest of the patients have to be operated on either because of a large, intraperitoneal haemorrhage or because the ectopic pregnancy does not show signs of resorption. The frequency of operation is independent of the supposed age of pregnancy and the size of the pelvic swelling on admission.

(2) When the Friedman reaction has become negative it is found that the risk of "catastrophe" is very slight. But only when clinical examination also indicates that the process has abated can we be absolutely sure that renewed internal bleeding will not occur.

(3) The follow-up shows no difference in postmorbid fertility between a group of conservatively treated patients and a comparable group of patients dealt with by operation. Operation should therefore be the treatment of choice in all early forms of ectopic pregnancy with a positive Friedman test.

If for some reason or other a woman with extra-uterine pregnancy has had the contralateral tube removed previously and she still desires to have a chance of pregnancy, however slight it may be, it is permissible to attempt conservative treatment, which in very rare cases may be followed by a normal pregnancy. But in such patients there will be a considerable risk of recurring ectopic pregnancy, and the patient should be informed of this.

(4) Patients with a negative Friedman test and a fair probability of an ectopic pregnancy should not generally be operated on. Exceptions from this rule are patients with considerable pelvic masses in whom operation may shorten the duration of the disease; furthermore operation should be performed in cases with an increasing or tender swelling, suggesting continued trophoblastic activity.

Summary

Sixty-eight cases of early ectopic pregnancy have been treated without operation, out of a consecutive series of 215 cases.

The results, immediate and remote, are described and conclusions are drawn as to the indications for this form of treatment.

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HAEMANGIOMA OF THE ENDOMETRIUM

BY

GRACE M. RITCHIE, M.B., Ch.B.

Senior Registrar in Pathology

AND

ALAN M. GILES, B.Sc., M.B., D.P.H., M.R.C.O.G.

Consultant Obstetrician and Gynaecologist, Stobhill General Hospital, Glasgow

HAEMANGIOMATA in varying forms are known to occur in many sites, e.g., the face, mucous membrane of mouth, subcutaneous tissue, and in various internal organs—liver, kidney, brain, etc. However, only a few examples of their occurrence in the uterus have been reported, and in the majority of these the lesion has taken the form of a cavernous angioma involving the myometrium with occasional extension into the endometrium. We have been able to trace only 1 case (Meyer, 1924), in which angiomatous tissue was found in endometrial curettings.

The following series of 10 cases in which angiomatous tissue has been identified in the endometrium has been drawn from analysis of 4,385 curettings taken over a period of 6 years. This total does not include curettings in which a definite diagnosis of carcinoma, tuberculosis or abortion could be made, and those few specimens in which the material was insufficient for diagnosis. In the 10 cases, with one exception for whom no details are available, all the patients were married, ranging in age from 34-51 years. One (Case 3) had had no full-time pregnancies or abortions, while the others were multiparous (para-2 to -11).

The following are brief clinical summaries and histological details.

CASE REPORTS

Case 1, aged 34, para-2, complained of increased menstrual loss, and slight white vaginal discharge since the last pregnancy in 1948. In 1951, after 6-weeks amenorrhoea, she had experienced lower abdominal pain of 3-days duration, and was admitted to hospital as a suspected ectopic pregnancy. Examination revealed a thickened, slightly tender left tube; the uterus was non-pregnant, and the Aschheim-Zondek test was negative. She was dismissed with a diagnosis of "chronic salpingitis, with possible rupture of a follicular cyst".

Menstruation returned and remained regular but heavy until August and September, 1953, when she had several episodes of sudden heavy vaginal bleeding, each lasting one day. Examination revealed a mobile, anteverted parous uterus, and at curettage on 25th September, 1953, a polyp, approximately 1 cm. in diameter, was removed from the cavity of the uterus.

Histologically much of the specimen showed a cavernous angioma. The central portion of the angiomatous tissues consisted of dilated venous channels with intense haemorrhage in the surrounding stroma. The edge of such a portion is illustrated in Fig. 1. The glands showed irregular proliferation at different parts, with no evidence of secretion.

In view of this finding total hysterectomy was performed on 30th October, 1953. Another simple polyp was found in the endometrium, but histologically this was adenomatous, and no evidence of residual angiomatous tissue was found in the specimen. No fibromyomata were present.

Recovery was uneventful and the patient's condition was satisfactory when she was last seen at the Follow-up Clinic.

Case 2, aged 41 years, had had 2 full-time spontaneous deliveries, 3 abortions and then a 27-weeks miscarriage in 1941. Subsequent menstruation was normal until 1947 when the patient had several heavy bleedings with the passage of clots. In May, 1947, curettage produced thick endometrium.

Histologically the endometrium was proliferative, with fibrosis, focal round cell infiltration and haemorrhage both within glands and in stroma. In several areas blood vessels were more numerous than could be related to parity or infection, and the appearances were at least suggestive of angioma.

Rather than hysterectomy, as she was excessively obese, she was given a menopausal dose of radium, but irregular bleeding recurred and further curettage was performed on 31st October, 1947. Histologically the endometrium was thin and the glands mostly atrophic,

but early proliferation was present in some areas with small haemorrhages in the stroma. There was no evidence of angioma.

Thereafter, the patient did not return until November, 1950, when she complained of dysmenorrhoea and post-menstrual brown discharge. Her menstrual cycle had continued and was 4–5/21 days with normal loss. On examination the uterus was bulky (cavity 9 cm.) and anteverted, with a small anterior fibroid. Curettage was performed and a small mucous polyp removed from the uterine cavity. Histologically this showed scanty, late secretory endometrium, and the polyp was adenomatous. There was no evidence of angioma.

Menstruation thereafter became heavy and irregular, and the patient finally consented to hysterectomy in May, 1951. The uterus contained numerous small intramural and subserous fibroids. Histologically the endometrium was proliferative, and at the edge of one section a small collection of thin-walled blood vessels was found (Fig. 2). The left ovary contained a corpus luteum and several simple follicular cysts. Recovery was uneventful.

Case 3, aged 45, complained in September, 1951, of vaginal haemorrhage of 6-weeks duration, with the passage of clots. She had been married for 22 years but had failed to conceive. Menstruation had been regular (4–5/28 days), with normal loss.

The uterus was slightly enlarged (cavity 7·5 cm.). A mass, approximately 6·5 cm. in diameter, was felt in the right ovary, and the presence of small submucous fibroids was suspected on curettage.

Histologically endometrial glands were scanty but proliferative, and the stroma bulky, with fibrosis and slight chronic inflammatory change. One portion showed a group of thin-walled blood vessels near the surface, while in another area numerous thick-walled vessels were seen (Fig. 3). The latter showed no fibrosis or hyaline changes in their walls, as is commonly found in the vessels of a parous uterus, and it would appear that both types of vascular abnormality could be explained only on the basis of angioma.

The patient was not seen again until January, 1954, when she was visited at her home in the course of this investigation. Menstruation, with scanty loss and regular cycle, ceased one year after curettage and no bleeding had since occurred. Examination was not permitted.

Case 4, aged 38, was admitted to hospital on 30th November, 1950, complaining of 3-days heavy vaginal bleeding.

Of her 11 pregnancies 7 were full-time and 4 were abortions, the last being an abortion at the twelfth week on 8th October, 1950. Bleeding stopped 5 days later. Heavy vaginal bleeding with large clots began on 27th November, 1950, persisting until admission on 30th November. After blood transfusion curettage was performed. The uterus was anteverted, bulky and mobile.

Histologically the material consisted of endometrium in the early secretory phase. The stroma showed only slight inflammatory change and numerous areas of large and small thin-walled blood vessels, suggesting the diagnosis of angioma.

Menstruation was normal for 6 months after dismissal but menorrhagia recurred and, after a further 6 months, curettage was performed at another hospital in January, 1952. The material showed proliferative endometrium with chronic inflammatory change in the stroma. There was much old and recent blood clot but no angiomatous material was seen.

She was recalled on 22nd October, 1953, during this investigation. Menstruation had been essentially normal (5–6/28–30 days) but occasionally the loss was heavy and prolonged as in September, 1953, when bleeding persisted for 4 weeks. On examination the uterus was anteverted (cavity 9 cm.). The adnexae were normal. Curettage was performed. Histologically the endometrium was proliferative with small haemorrhages, patchy fibrosis, and diffuse round cell infiltration in the stroma. No vascular abnormality was apparent.

The patient menstruated normally for 4 days from 30th November, but, on 17th December, 1953, scanty bleeding recurred and continued until seen on 31st December, 1953. Hysterectomy was refused. She was seen again on 8th February, 1954. Menstrual loss was still heavy.

Case 5, aged 42, had had 6 spontaneous deliveries, the last 5 years previously. Since then she had complained of stress incontinence of urine, yellow vaginal discharge and headaches. The menstrual cycle had been regular, 3–4/21 days, with normal loss.

On examination in March, 1950, the uterus was bulky and retroverted. A small polyp protruding through the cervix was removed by torsion (Spec. A). Curettage (Spec. B) and a Donald-Fothergill repair were performed. Specimen A: a small part of the material showed a clearly identifiable simple cervical adenoma, but more than three-quarters of the specimen consisted of angiomatous tissue of mixed capillary and venous type, with superficial inflammatory change. In the background, particularly at the periphery, endometrial stroma with an occasional gland, could be identified. Specimen B: the curettings showed the proliferative phase, with acute and chronic inflammatory change in the stroma.

Since her operation, the patient's periods have been slightly irregular, but without heavy loss or inter-menstrual bleeding. She is now at the menopause.

Case 6, aged 51 years, complained of vaginal bleeding of 14-days duration in March, 1950. The first 4 of her 7 pregnancies terminated at term in spontaneous deliveries; then followed 3 abortions, the last in 1943. Menstruation had been regular, 3–4/28 days, but with scantier loss in recent years.

On 17th March, 1950, there was heavy vaginal bleeding, with clots and slight abdominal pain, persisting until admission on 30th March, 1950. On examination, the uterus was enlarged to the size of a 3-months pregnancy, and a subserous fibroid was felt on the right side of the body. On curettage (31st March, 1950) several scraps of endometrium were obtained, the largest of which had an

FIG. 2

Section of uterus showing a minute venous angioma at the edge of the endometrium. ×100.

FIG. 1

Peripheral portion of specimen showing collection of greatly dilated blood vessels. ×100.

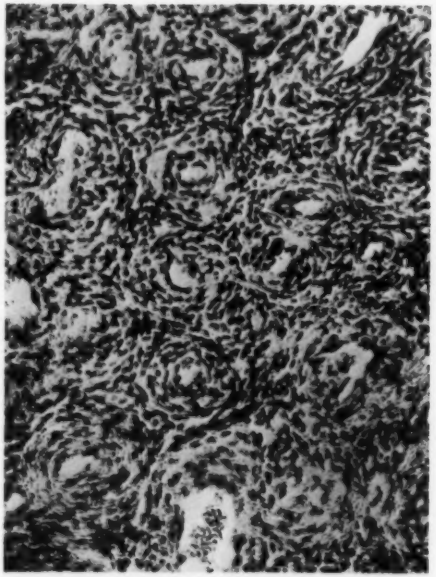

FIG. 3

Collection of young blood vessels, with thick walls, many nuclei and no degenerative changes, occurring in endometrium. ×175.

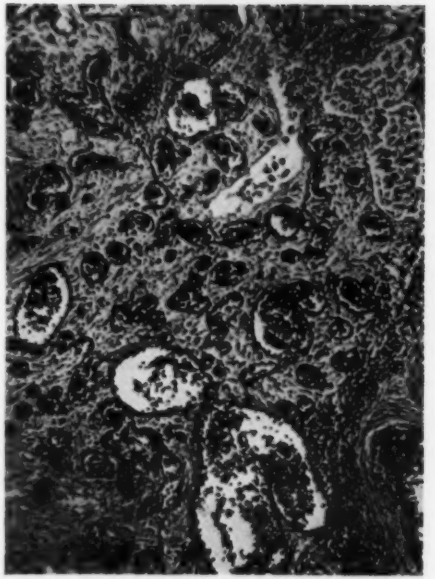

FIG. 4

Portion of angioma containing two endometrial glands with desquamated lining, one thick walled blood vessel, several venous channels and numerous capillaries. ×100.

angiomatous appearance similar to that in Specimen A of Case 5, except that the blood vessels were in the main thicker-walled. The rest of the endometrium showed the proliferative phase, with marked oedema and polymorph infiltration in the stroma.

After dismissal the patient had no further bleeding until 5th July, 1950, when heavy bleeding began, necessitating panhysterectomy on 20th July, 1950, after which the patient made an uneventful recovery.

The bulky uterus contained many small fibroids. A supracervical fibroid (5 cm. diameter) was present on the right side. Histologically no residual angiomatous tissue was seen. The endometrium was proliferative, of a non-secreting menopausal type. The myometrium showed hyaline fibrosis. The cervix showed numerous Nabothian follicles and chronic inflammatory changes.

The ovaries contained several corpora albicantia, some of cystic dimensions with abundant haemosiderin pigment in the wall. The tubes showed no abnormality.

Case 7, aged 37 years, had had 1 abortion followed by 3 spontaneous deliveries, the last in 1944. Thereafter, menstruation was normal until January, 1950, since when the cycle had become 8–10/14–21 days, with clots, heavy loss and slight dysmenorrhoea.

On 17th June, 1950, the uterus was anteverted and of normal size. Tubes and ovaries were normal. A small cervical erosion was seen. During examination at the Gynaecological Clinic, a piece of tissue protruding through the cervix was detached.

Histologically this bulky material consisted of endometrium in which numerous large and small thin-walled blood vessels were present, suggesting the diagnosis of angioma. The stroma and glands were largely obscured by recent haemorrhage but parts showed proliferative endometrium.

Curettage 10 days later produced endometrium in the proliferative phase, with fibrosis and focal round-cell infiltration in the stroma. No evidence of decidua or further angiomatous material was seen.

During the following 3 years the patient continued to experience menorrhagia, severe at times, with an irregular cycle, but failed to report to the Clinic. She was recalled during the present investigation. Laparotomy was advised and total hysterectomy was performed. Tubes and ovaries appeared normal and were left in situ. The patient made an uneventful recovery.

In the uterus ($9 \cdot 5 \times 6 \times 4 \cdot 5$ cm.) there were no fibroids though the myometrium was thickened. A polyp ($2 \cdot 25 \times 1 \cdot 5 \times 0 \cdot 5$ cm.) arose from the endometrium at the fundus. Histologically the endometrium was in the late proliferative phase with fibrosis and diffuse and focal round cell infiltration in the stroma. The simple adenomatous character of the fundal polyp was confirmed. Thorough examination of all parts showed no evidence of angioma.

Case 8, aged 44 years, had had 3 spontaneous full-time deliveries, the last in 1942. She was admitted for investigation in August, 1950, with a complaint of irregular and heavy periods (5–7/14–21 days) for the previous 2 years. Occasionally the loss had taken the form of sudden severe haemorrhages, and bleeding had been continuous for the 5 weeks prior to admission. The uterus was slightly enlarged (cavity 7·5 cm.), anteverted, firm and mobile. After blood transfusion, curettage was performed.

Histologically the material showed marked variation in size and shape of the non-secreting proliferative glandular acini, many of which were greatly dilated. Parts of the stroma were haemorrhagic, but in addition, in one area, the appearances were those of a venous angioma.

An artificial menopause by X-ray therapy was advised, but refused. After 2 further episodes of bleeding in September and October she was readmitted on 21st October. Curettage showed nothing significant but, in view of her age and refusal to have a hysterectomy, a menopausal dose of radium was inserted into the uterine cavity. On 10th November one day's bleeding occurred, but the loss was not heavy. She has not bled since.

Case 9, aged 37, was admitted to hospital on 28th February, 1952, after 5-weeks continuous heavy vaginal bleeding. She was very anaemic. In 1939 she had had "cysts removed from both ovaries", and in 1945 had a forceps delivery of a full-time foetus. Menstruation had always been irregular and her reproductive history was rather indefinite, but she believed that she had had 5 "pregnancies" subsequent to 1945 all terminating in "abortion about the third month".

In 1950, after 3-months amenorrhoea, during which time she thought she was pregnant, she had lower abdominal pain, with bleeding which persisted for one month. Curettage then showed proliferative endometrium, with slight diffuse round cell infiltration in the stroma, but no significant fibrosis; no retained products of conception were present. In at least two areas dilated veins were seen just under the surface; in one part there was also slight acute inflammatory change, but the other part showed no inflammation and suggested the diagnosis of angioma.

Thereafter menstruation was irregular. After 2-months amenorrhoea she had 3 heavy periods with clots and lower abdominal pain. Curettage on 18th September, 1952, produced thick endometrium in the proliferative phase, with patchy dilatation of glands and small haemorrhages and oedema in an otherwise compact stroma. In one area the appearances were those of a capillary angioma, with several large venous sinuses as well.

After this curettage she had 4-months amenorrhoea followed by heavy vaginal bleeding, passage of clots and pain in the left iliac fossa. Bleeding continued for 5 weeks and she was admitted to hospital where total hysterectomy with left salpingo-oöphorectomy, was performed on 4th March, 1953. Adhesions were present around the tube and ovary.

The uterus, 10 cm. in total length, showed thickening of the myometrium, but no fibroids. Histology showed several minute polypi; the tip of the largest was composed of angiomatous tissue, while in another, intense haemorrhage obscured structural details. Recovery was uneventful.

Case 10. No clinical details are available but the material was protruding from the cervix. Histologically it consisted of oedematous endometrial stroma with few glands but many large and small dilated blood vessels (Fig. 4).

Discussion

Haemangiomata are described as hamartomata or vascular malformations rather than true tumours; many are obvious at birth or are noticed soon afterwards, but those of the deeper tissues may not be discovered until later in life (Willis, 1948). In general they are of slow growth and benign course (Ewing, 1931). They may occur in varying forms, depending on the type of blood vessel forming the main component, though mixed varieties are common. Brief reference only, devoid of detail, is made in standard textbooks to their possible occurrence in the uterus, and available literature also contains relatively few recorded accounts. However, in 1867 Virchow, quoted by Horgan (1930), reported a case of cavernous haemangioma involving the uterine wall; he stated that it was rare if telangiectases were excluded, but gave no details of this latter variety. Since then a number of cavernous haemangiomata have been recorded and these have been comprehensively reviewed by Horgan (1930) and Marsh (1950). In the main they have involved the myometrium with occasional extension into the endometrium, while a few have taken the form of submucous polypoid haemangiomata. Brodersen (1928) has reported a case of angioma of the mucous membrane of the uterus in a girl of 18 years in which the uterine bleeding over a period of 2 years was so severe as to necessitate supra-vaginal hysterectomy. Examination of the uterus disclosed a "dime-sized" haemangioma in the fundus.

In 1925 Meyer presented 4 cases of telangiectases of the uterus. He described the lesions as circumscribed, irregularly shaped, blood red tumours in the inner portion of the myometrium. Two of them extended into the mucosa, and the largest of the 4 tumours did not exceed 4 mm. in diameter.

In 2 of these cases myomata were also present, and in 1 of these there was also a small polypoidal carcinoma at the fundus. Neumann (1930) has also reported 2 cases of focal capillary growths in the uterine wall, 1 immediately under the serosa and the other under the mucosa. Myomata were also present but the vascular lesions were not intimately associated with the myomatous areas.

In only 1 instance (Meyer, 1924) has angiomatous tissue been found in curettings. This patient, a woman of 62, had had heavy bleeding for which curettage was performed. The angioma was capillary in type; no sign of persisting inflammation or infiltration of any sort was demonstrable, but Meyer believed that the vascular lesion might possibly have originated in old granulation tissue.

It is indeed surprising how little attention has been paid to haemangioma of the endometrium in view of the large numbers of curettings examined routinely throughout the world. It is all the more remarkable as the cyclical growth changes in the endometrium, its potential capacity for greatly increased vascularity in the pregnant state and the not infrequent presence of infection are all factors which appear favourable to the development of vascular anomalies. However, as the lesions we have found in our present series are small and mostly superficial, it is also probable that many examples are shed in the menstrual detritus.

It will be apparent that the diagnosis of haemangioma must be made on a histological basis as there are no reasonable clinical grounds for suspecting its presence. However, before a definite diagnosis can be made, it is important to exclude other physiological and pathological processes which in themselves might induce increased vascularity.

Firstly, in pregnancy the uterine vessels show enormous increase in size, with increase in elastic tissue. In the present series, in 7 of the cases the average time between the last pregnancy and the histological diagnosis was just over 6 years, in 1 (Case 4) it was 7 weeks, in another (Case 3) the patient had failed to conceive during her 22 years of married life, and in the last (Case 10) no clinical details were available. In Cases 3 and 4 further elaboration of this point is required.

In Case 3 no pregnancy at all had occurred yet histology showed two different vascular anomalies—a superficial area of thin-walled blood vessels similar to that found in several of

our specimens (cf. Fig. 1), and in another part (Fig. 3), at a deeper level, a poorly circumscribed collection of blood vessels with much thicker walls, in size and pattern resembling those associated with parity. The vessel walls showed no fibrous or hyaline change; the groups were much more numerous and more diffusely spread and these appearances occurring in a woman of 45 years near the menopause would disprove their association with parity and suggest a recent origin.

In Case 4, despite the short lapse of time between what appeared to be a definite abortion and the diagnosis of angioma, histology revealed no retained products of conception and there was no indication that the angioma had originated in placental tissue nor was its pattern comparable with a group of thick-walled blood vessels persisting at the site of implantation.

Thus, care must be exercised in differentiating between vessels persisting at the placental site and those of true angioma.

Secondly, several authors have also stressed the association between fibromyomata and angiomata, but the vascular lesions have shown no intimate association with the fibromyomatous areas. In the present series the presence of fibroids was confirmed after hysterectomy in 2 cases (2 and 6), and was suspected on curettage in Case 3. In Case 6 no residual angiomatous tissue was seen, and in Case 2 the small vascular lesion (Fig. 2) found was not associated with the fibroids present.

Thirdly, infection, especially if acute, may also be responsible for increased vascularity. In the present series patchy, superficial, acute inflammatory change was present in several of the specimens, but this inflammation was most intense at a distance from the angiomatous areas or occurred superficially when the angiomatous material was polypoid. Furthermore, in increased vascularity of inflammatory origin the vessels consist partly of pre-existing capillaries in a dilated state and partly of newly-formed small vessels with plump cells in the walls, neither being comparable to the vessels illustrated in these cases. Finally, in 2 specimens (Cases 4 and 10) evidence of inflammation was entirely lacking yet these 2 provided our best examples of haemangioma.

When such physiological and pathological demands for increased vascular supply can be excluded it is reasonable to assume that the vascular lesions are indeed haemangiomata.

Once the diagnosis is established it is quite a different matter to assess its clinical significance. In the present series the problem is further complicated by the co-existence of other grosser uterine lesions and, in view of this, further analysis of the pathological findings seems desirable.

In 3 cases (2, 3 and 6) fibroids were present, and in addition Cases 3 and 6 were also menopausal; in Cases 1 and 7 endometrial polypi were found; in Cases 8 and 9 the presence of slight irregular hyperplasia and dilatation of glands was noted; and in Case 4, who had had 11 pregnancies, a diagnosis of "subinvolution" could be made. In all of these the main symptom was heavy bleeding, but it is interesting to note that in Case 5 menstruation was normal, with normal loss, and the symptoms were directly referable to her prolapse, yet histology showed a well-defined haemangioma.

On the other hand, in Brodersen's case, the uterine bleeding was sufficiently severe to necessitate hysterectomy, but on examination the only lesion found was a haemangioma of the endometrium. It therefore seems reasonable to conclude that the clinical significance of haemangioma may vary from that of a small, interesting but academic finding to that of a serious pathological lesion necessitating major surgery.

Accordingly, it is suggested that in the differential diagnosis of uterine bleeding the possibility of a haemangioma of the endometrium should be considered.

Summary

A series of 10 cases of haemangioma of the endometrium is reported, with brief case notes, details of histological appearances and discussion of their clinical significance.

Attention is drawn to the scanty references available.

It is suggested that haemangioma of the endometrium must be included in the differential diagnosis of uterine bleeding.

Acknowledgments

Our thanks are due to Dr. J. C. Dick, of the Department of Pathology, Stobhill General Hospital, for much helpful guidance, to Dr. McKay Hart and Dr. A. Freeth of Western District Hospital for access to clinical records and material of 2 cases, and to the other clinicians and pathologists who assisted in confirming previous incidents and findings in several of the cases.

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THE BEHAVIOUR OF THE BLOOD PRESSURE IN PREGNANCY ASSOCIATED WITH COARCTATION OF THE AORTA

BY

H. G. DIXON, M.B., B.S., M.R.C.O.G.

Registrar, Department of Obstetrics and Gynaecology
Postgraduate Medical School and Institute of Obstetrics and Gynaecology
University of London

AND

RONALD HARTLEY, M.R.C.P.

Consultant Physician
British Hospital for Mothers and Babies

MUCH work has been done on the coincidence of pregnancy and coarctation of the aorta, but little attention has been paid to detailed blood pressure readings taken throughout the cyesis and parturition. Such readings help to assess the potential danger of rupture of the aorta and also offer evidence as to the aetiology of the brachial hypertension in subjects with coarctation by comparing the readings with similar ones occurring in pregnant women suffering from essential hypertension. This paper offers a report of the behaviour of the blood pressure during the course of 4 pregnancies occurring in 2 women with coarctation of the aorta.

THE HAEMODYNAMICS IN NORMAL PREGNANCY AND IN THE PREGNANT ESSENTIAL HYPERTENSIVE

The changes in haemodynamics occasioned by pregnancy have been the subject of many communications to the literature extending over the past three decades and certain basic facts are now accepted.

A rise in blood volume occurs. Using P^{32} labelled red blood cells, Berlin *et al.* (1953) have shown this increase in volume to be over 30 per cent. Hamilton (1949) using the cardiac catheter found an increase in cardiac output of 25 per cent by the twenty-sixth to the twenty-ninth week. A fall in blood viscosity was confirmed by Hamilton (1950).

At the time of maximum cardiac output there is a normal or low blood pressure first noted by Hare and Karn (1929). The fall in blood viscosity is not sufficient to account for this and it is concluded that a slight fall in the mean peripheral resistance must occur. This lowering of peripheral resistance is probably due to the introduction of the vascular uterus into the circulation. Whether or not the highly vascular utero-placental area acts as an arterio-venous shunt, a possibility suggested by Burwell (1938) and criticized by Kellar (1950), does not concern this paper.

The haemodynamics of essential hypertension have been the subject of much study by Goldring and Chassis (1944), who describe no increase in blood volume, cardiac output or blood viscosity, but a great increase in the mean peripheral resistance.

Hamilton (1951) found the increase in the cardiac output in the pregnant hypertensive to be similar to that found in the normal pregnant woman; thus, a rise in blood pressure might be expected to result when a hypertensive becomes pregnant. Reid and Teel (1939) found, however, a fall in blood pressure to occur during pregnancy in the hypertensive patient. That this phenomenon does occur in at least one-third of patients with fixed essential hypertension has been confirmed by Chesley *et al.* (1947) and by Browne (1947).

The suggested cause for this paradoxical effect of pregnancy on the blood pressure in essential hypertension is, as in normal pregnancy, a fall in the mean peripheral resistance.

Hypertension in Coarctation of the Aorta

The original theory to account for brachial hypertension in coarctation of the aorta was that of mechanical obstruction. The brachial hypertension is generally systolic but the diastolic pressure may be raised to some degree. Steele (1941) has shown that, while the femoral systolic pressure may be low or normal, the femoral diastolic pressure is actually high, and from this he concludes that there is a generalized increase in peripheral resistance in coarctation of the aorta and that this accounts for the high brachial blood pressure. Bing *et al.* (1948) did not agree with this and thought that the height of the diastolic pressure in both upper and lower limbs could be explained by the damping of the pulse wave by the obstruction and by the arterial collaterals.

The third theory is that of hypertension secondary to renal ischaemia. Friedman *et al.* (1941) showed that of 6 cases of coarctation all showed a partial renal ischaemia, and it is true that post-operatively the blood pressure will frequently not return to normal if the obstruction has been left too long. On the other hand, Maycock (1937) described a case where stenosis of the aorta 1·5 cm. below the renal artery caused a rise in brachial blood pressure to 210/89. The exact mechanism of the brachial hypertension and its limitation to the upper half of the body is not known, in spite of animal experiments.

Case Reports

Case 1. Mrs. J. W., aged 23 years and gravida-2, during her first pregnancy, in 1948, had been diagnosed as suffering from subaortic stenosis. The pregnancy had

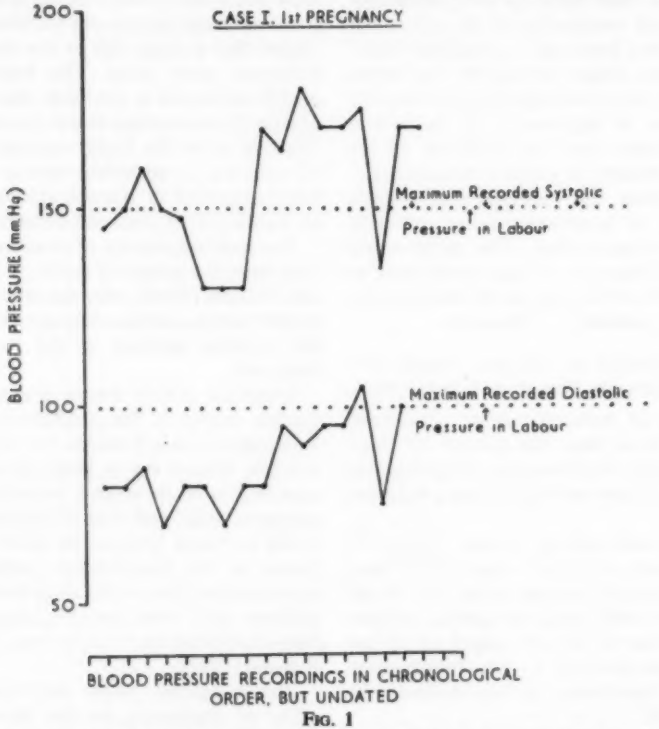

Fig. 1

Case 1. Chart of blood pressure recordings during first pregnancy with maximum recorded pressure in labour superimposed.

been uneventful and had ended in the spontaneous delivery of a 6 pounds 12 ounces (3,370 g.) infant after a 7¼ hour labour.

The original records of this pregnancy are unfortunately not available and, although there are many blood pressure recordings in the précis that had been retained, these are undated. They are given in order and cover the whole pregnancy, so that it has been thought permissible to present them in graphic form. It is known that the highest recorded blood pressure in labour was 150/100.

After this delivery a diagnosis of coarctation of the aorta was made and confirmed by angiocardiography.

In her second pregnancy, she first attended the antenatal clinic when 8-weeks pregnant, the last menstrual period being on 16th January, 1950. She felt well and became breathless only on severe exertion. On examination she presented no abnormality other than in the cardiovascular system. The left ventricle was enlarged, the apex beat being ½ inch (1·25 cm.) outside the midclavicular line. A moderately loud, blowing systolic murmur was heard all over the praecordium and over the back of the chest as far down as the lower angles of the scapulae.

The blood pressure in both arms was 170/90. No pulses could be felt in the legs. Antenatal progress was uneventful, the blood pressure falling to the region of 140/80.

When 30-weeks pregnant she was admitted for rest because of dyspnoea on normal exertion. This symptom cleared slowly after bed rest. During her 22-day stay in hospital the blood pressure averaged 150/80. Haemoglobin estimation was 70 per cent (10·3 g.).

At 38 weeks she was again admitted with dyspnoea. A blood count showed the haemoglobin to be 58 per cent (8·6 g.) with a packed cell volume of 30 per cent and a colour index of 0·63.

The blood picture was of a microcytic hypochromic anaemia. She was treated with rest, intravenous iron (100 mg. daily) to a total of 1·06 g. and ascorbic acid 100 mg. t.d.s.

On 20th October, 1950, she went into spontaneous

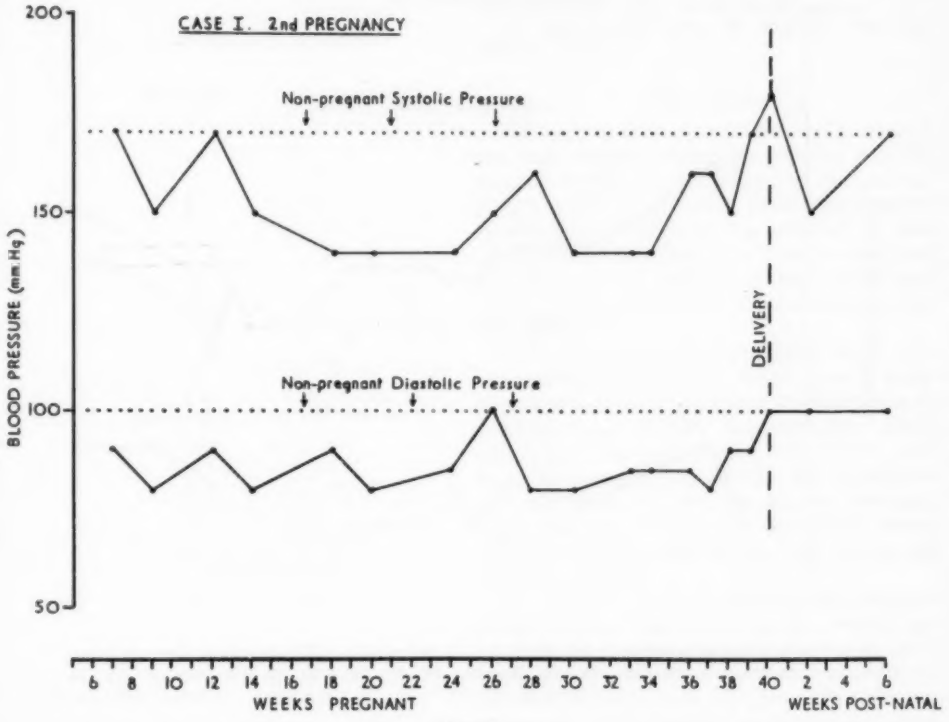

FIG. 2

Case 1. Chart of blood pressure recordings during second pregnancy and labour with non-pregnant recording superimposed.

labour. The blood pressure was 160/100. She delivered spontaneously 5 hours 25 minutes later, after a 2nd stage of 10 minutes. The blood pressure during the last ½ hour of the first, and throughout the 2nd stage was 180/100. The 3rd stage was normal. The infant weighed 7 pounds 9 ounces (3,780 g.) and was healthy.

Two and a half hours after delivery the blood pressure was 150/90, the pulse 84 and the patient very well.

The puerperium was uneventful, the blood pressure remaining in the 150/90 range. For fear that early ambulation might cause too sudden a rise she was kept in bed until the 12th day, but no sharp rise did in fact occur. Lactation was normal. On 8th December, 1950, the woman was seen at the postnatal clinic. She was well. Her cardiovascular signs were unchanged. The blood pressure was 170/100. Gynaecological examination revealed no abnormality but arrangements were made for her subsequent admission to the gynaecological unit for sterilization.

At the time of writing, her blood pressure is 200/110.

Case 2. Mrs. M.V., age 19 years, was a primigravida. When first seen at the antenatal clinic on 31st May, 1950, she gave the date of the last menstrual period as 12th March, 1950, the estimated date of delivery being 19th December, 1950. She gave no history of any disease or operation and regarded herself as quite normal.

Examination revealed a well developed girl with some leucodermic patches on the neck. She had a normal pregnancy of 12-weeks duration. Examination was normal apart from the cardiovascular system. There was a harsh thrill, felt over all the praecordium, with a harsh systolic murmur audible over the front and back of the chest and conducted up into the neck. There was no clinical cardiac enlargement. The blood pressure in both arms was 160/70. The radial pulses were strong and equal, the femoral palpable, but weak and the dorsalis pedis pulses impalpable.

Dyspnoea was induced by alternate sitting and lying 8 times and the patient stated that she often became dyspnoeic on climbing the stairs to her top floor flat.

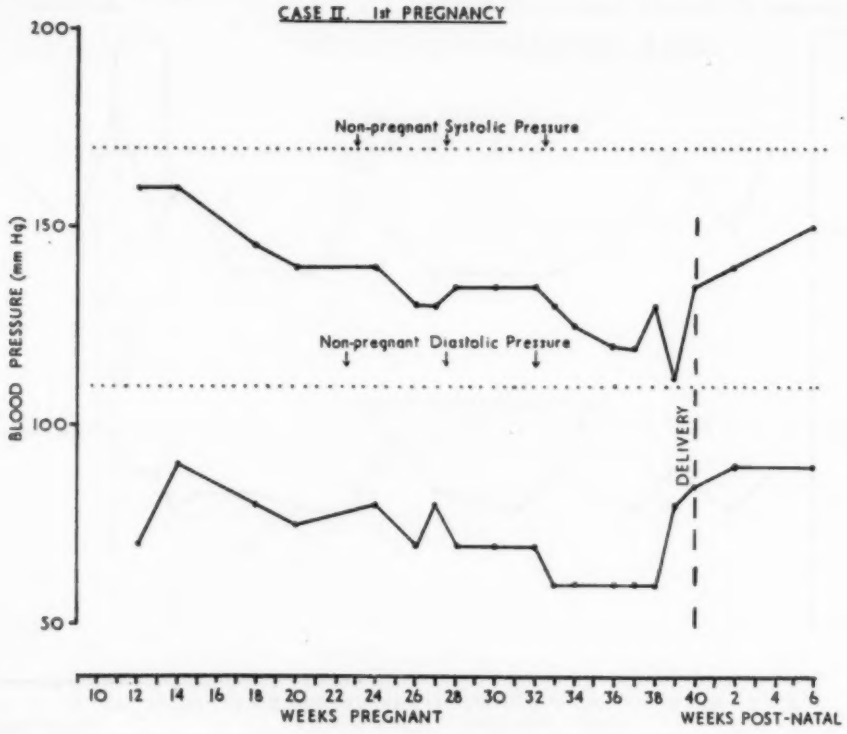

FIG. 3

Case 2. Chart of blood pressure recordings during first pregnancy and labour with non-pregnant recording superimposed.

A diagnosis of coarctation of the aorta was made.

Her obstetrical progress was normal. The blood pressure remained at about the same level until the 20th week, when it had fallen to 130/70. At the 26th week it was 130/70 but the patient was complaining of dyspnoea on walking 20 yards. She was therefore admitted to hospital for 9 days.

After this, until the 39th week, she continued well. The blood pressure recordings became progressively lower, being 112/80 at 39 weeks when she was readmitted for rest and assessment before delivery.

The foetus was presenting by the head and, although the head was not engaged, there was no cephalo-pelvic disproportion. She remained well, the blood pressure fluctuating between 140 and 110 systolic and 90 and 70 diastolic.

On 23rd December, 1950, a simple oil, bath and enema induction was given and she went into labour 12 hours later.

The cervix became fully dilated after 6½ hours labour. The head was low and a forceps delivery under pudendal block anaesthesia was performed. A living female infant of 6 pounds 9 ounces (3,280 g.) was delivered with the aid of an episiotomy which was afterwards sutured.

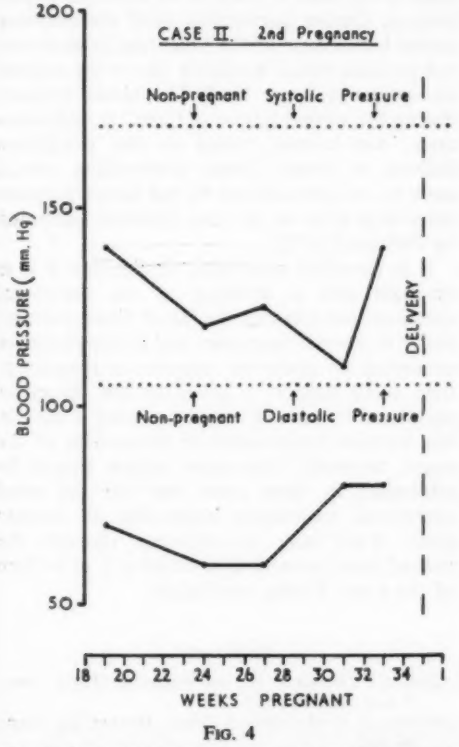

FIG. 4

Case 2. Chart of blood pressure recordings during second pregnancy with non-pregnant recording superimposed.

The blood pressure during delivery was recorded as 135/85 and after delivery was 120/80, the pulse rate being 90. The puerperium was quite uncomplicated, the blood pressure rising to 140/90 on discharge on the 16th day. Six weeks after delivery the patient was seen at the post-natal clinic. The physical signs were unchanged. The blood pressure was 140/90. It is known to have risen to 170/110 2 months later.

She was referred to a birth control clinic and arrangements made for further cardiological investigation. Angiocardiography confirmed the coarctation.

The patient did not practise the birth control that was advised and attended the clinic again on 9th January, 1952, when 19 weeks pregnant. The blood pressure at that time was 140/70 and her progress was comparable with that during the previous pregnancy. The blood pressure recordings are shown on the attached chart. Unfortunately she had a precipitate delivery at home after 35-weeks gestation, delivering a live 4 pounds 14 ounces (2,211 g.) infant, which survived.

The blood pressure after this pregnancy rose once again to 170/110.

DISCUSSION

The literature on coarctation and pregnancy has been reviewed within the past few years by Benham (1949) in this country, by Soulie *et al.* (1951) in France and most recently in America by Pritchard (1953), who has collected 77 cases of coarctation and pregnancy from the literature extending back to 1859 and added 2 of his own. The total, therefore, with the 2 cases recorded here reaches 81.

This is a surprisingly low figure when it is remembered that Fawcett (1905), from a study of autopsy material, reported the incidence of coarctation as 1:1,000 post-mortems. Lewis (1933) gives the male:female ratio as 8:1, and it can be assumed from this that the incidence is not less than 1:5,000 women, an incidence suggesting that, in England and Wales alone, over 100 women suffering from coarctation are delivered annually.

To account for this discrepancy, Benham (1949) quotes Evans as giving the average age of death of sufferers from coarctation as 28·7 years and suggests that the female patients do not live long enough to reproduce. This gloomy prognosis is not, however, supported by Lewis (1933, 1942) nor by Bramwell (1947) and it does not seem that Benham's explanation is adequate.

A syndrome in which coarctation and ovarian agenesis coexist has been described by Albright *et al.* (1942) and Wilkins and Fleishmann (1944). Goldman *et al.* (1949), in supporting these workers, claimed that 4 out of 5 of his cases of coarctation showed clinical evidence of ovarian insufficiency. It seems reasonable to suggest this as a cause for the small number of pregnancies in coarctation patients.

It may be that a number of cases of coarctation are diagnosed as essential hypertension. The fact that most of the undiagnosed cases deliver normally while the more severe or fatal cases are likely to be recorded, may have provided an exaggerated view of the gravity of coarctation as a complication of pregnancy (Benham, 1949).

Eight patients have died during pregnancy, an incidence of 10 per cent but, as Pritchard (1953) points out, during the last 20 years the mortality has been only 6 per cent. This compares not unfavourably with figures for rheumatic heart disease (Grade 2) with pregnancy given by Morgan Jones (1951).

The danger that sets coarctation apart from the other heart lesions encountered in obstetrical practice is that of rupture of the aorta. There is of course the danger of rupture of associated aneurysms. This association is said, by Morgan Jones (1951), to occur in one-third of cases of coarctation. The factors concerned with rupture of these aneurysms are the same as those influencing the aorta; only the aorta will be considered here.

It is possible that there are factors operating in pregnancy that make the risk of rupture more likely than in the non-pregnant state.

Joule (1949) in a paper concerning dissecting aneurysms describes a case of rupture of the aorta, not associated with coarctation, occurring 3 weeks after delivery. He makes the observation that spontaneous rupture of the aorta in coarctation probably does not occur except in the presence of cystic medial necrosis of the aorta. He postulates that this condition, more common in thyroid insufficiency, may be likely to arise in pregnancy if the thyroid fails to undergo sufficient hyperplasia to meet the extra demands of the foetus. The antenatal fatality reported by Kinney *et al.* (1945) did in fact show cystic medial necrosis of the aorta, and it is possible that a case could be made for the administration of thyroid to these cases during pregnancy.

The great danger stressed by almost all authors is that of a rise of blood pressure associated with pregnancy and more especially with labour proving too great for the aortic wall to withstand.

Conclusions

This study suggests that the blood pressure during pregnancy in patients with coarctation behaves in the same way as does the blood pressure in normal pregnancy and in essential hypertension. That is to say, there is a dramatic fall in the middle trimester with a tendency to rise again towards the end of pregnancy. This secondary rise did not however seem to be so marked in these 2 cases as in essential hypertension. During parturition itself the response varied but in none of the 3 recorded labours was the pressure raised markedly above the normal non-pregnant upper level. The blood pressure during the second labour of Case 2 is, unfortunately, not known, owing to the precipitate delivery at home. These observations would seem to be substantiated by the blood pressure recordings given in the case histories presented by Pritchard (1953).

It is therefore concluded, firstly, that if it is accepted that a lowering of the peripheral resistance accounts for the fall in blood pressure found in normal pregnancy and in hypertensives exhibiting an optimum response to pregnancy, then some support is given to the theory of peripheral vascular resistance playing a part in the brachial hypertension in coarctation of the aorta. Secondly, Caesarean section should be performed in these cases only for the usual obstetrical indications applicable to cardiac cases. They may be delivered through the normal passages with little added risk of rupture of the aorta during parturition.

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DIVERTICULUM OF THE FEMALE URETHRA

BY

J. B. NEL, M.B., Ch.B.

Department of Obstetrics and Gynaecology, University of Cape Town

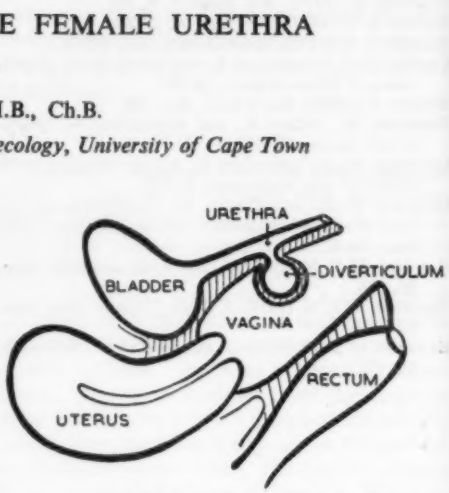
MEDICAL problems are often solved by the combined effort of different branches of medicine. Likewise do micturition and its disorders need the cooperation of the clinician, physiologist and pathologist. The mechanism of micturition is far from solved. Jeffcoate and Roberts (1952), and some workers before them, have opened a new avenue of approach, namely, disturbance of the posterior urethro-vesical angle. Once it is known how urination is controlled, the treatment of the distressing symptom of stress incontinence will become simplified. The extensive investigations of stress incontinence and lower urinary tract physiology are proof of the importance of this disabling condition. It is, therefore, perhaps not out of place to discuss a less well-known cause of stress incontinence, namely diverticulum of the urethra and to report a case admitted to the Groote Schuur Hospital during the year 1953.

Diverticulum of the female urethra is easy to diagnose and relatively simple to treat. However, the diagnosis is often overlooked, no doubt because of its infrequent occurrence and of the failure to examine the urethra properly.

In anatomical abnormalities of the urethra three terms are used somewhat indiscriminately, viz., diverticulum of the urethra, urethrocoele and urethral prolapse. The following short description should show that they are not synonymous.

A diverticulum (Fig. 1) is a pouch of a portion of the urethro-vaginal septum communicating with the urethral canal; the opening into the urethra may be wide or narrow (Krieger and Poutasse, 1952; Downer and Virgilo, 1945).

A urethrocoele (Fig. 2) is a generalized sagging of the urethra, resulting in a bulging of the related anterior vaginal wall (Lowrie, 1952),



DIVERTICULUM OF THE URETHRA.

FIG. 1

the cause being loss of fascial and muscular support (Mayers, 1938).

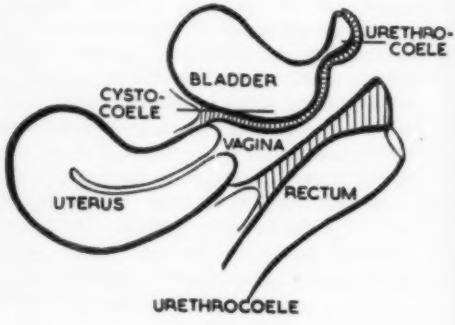


FIG. 2

Prolapse of the urethra (Fig. 3) is a protrusion of the urethral mucous membrane through the external urinary meatus (Mayers, 1938).

The *incidence* of urethral diverticula is difficult to ascertain. The following are some of the series

TABLE I

Incidence

Author	Clinic	Period: years	Date	Number
Counseller	Mayo	—	1949	71
Wharton and Kearns	Johns Hopkins	60	1950	30
Menville and Mitchell	—	20	1944	13
Higgins and Rambousck ..	Cleveland	—	1945	12
Furniss	—	—	1935	10
Schmitz	—	10	1939	8
Cullen	—	—	1894	1
Johnson	—	10	1938	0
„	—	The next year	—	9

reported: Table I alludes to series from different clinics and Table II to cases reviewed from the literature.

In 1938 Johnson reported that over a 10-year period in one hospital the diagnosis did not appear in any of the 140,000 admissions, but

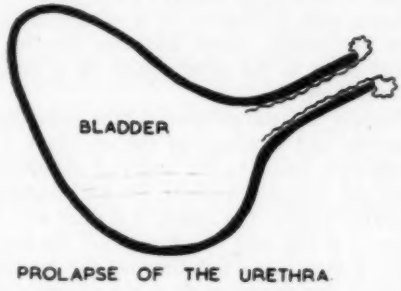


FIG. 3

TABLE II

Cases Collected from the Literature

Author	Date	Number
Schmitz	1939	100
Menville and Mitchell	1944	80 (Reviewed)
Cullen	1894	37

after demonstrating 2 cases to three urologists, 9 cases were diagnosed in one year. Notwithstanding the fact that a patient was treated for this condition as early as 1786 (quoted by Hunner, 1938), it has only been during the past 15 years or more that its extreme rarity has been questioned.

The average *age of patients* lies between 38 and 41 years (Counseller, 1949). In one series of 71 cases it was 38·8 years (Menville and Mitchell, 1944).

Aetiology: The consensus of opinion is that in most instances urethral diverticula are acquired (Curtis, Anson and McVay, 1938; Everett, 1947; Furniss, 1935; Higgins and Rambousck, 1945; Menville and Mitchell, 1944; Townsend, 1938; Pratt, 1938; Shivers and Cooney, 1934; Dodson, 1950; Kirby and Reynolds, 1949; Schmitz and Nelson, 1939), However, some authors favour a congenital origin (Counseller, 1949; Jarecki, 1914; Johnson, 1938). Those advocating the latter theory believe that these congenital diverticula or cysts may be symptomless and that trauma and infection are largely responsible for the symptomatology. There is no definite proof, as yet, of its aetiology; one or more of the factors in Table III may be involved.

Of the acquired conditions, the following may be mentioned. Firstly, perforation of the urethra. Trauma may be limited to the muscularis. It can be produced by childbirth, especially repeated childbirth, coitus, rough packing of the vagina, and instrumental deliveries and instrumentation of the urethra. It must be emphasized that obstetrical trauma, however, is more likely to result in a urethrocoele than in a diverticulum (Huffman, 1951). An infection of a paraurethral gland may lead to a sealing off of the opening into the urethra, formation of an abscess and, as a result of increased tension, rupture may occur with re-establishment of the communication with the urethra. Chronic urethritis may be

TABLE III

Aetiological Factors

A. Acquired	1. Perforation of urethra	(a) Trauma to urethra. (b) Rupture of paraurethral abscesses. (c) Rupture of blood cysts.
	2. Local dilatation of urethra	(a) Urethral calculus. (b) Urethral stricture. (c) Scar tissue traction.
B. Congenital	1. Gärtner's duct. 2. Faulty union of primal folds. 3. Cell rests. 4. Vaginal wall cysts—Müllerian remnants. 5. Congenital dilatation of paraurethral ducts.	

the cause of this infection (Routh, 1890) and, indirectly, cervicitis (Folsom and O'Brien, 1945). Rupture of blood cysts into the urethra may occur. Secondly, local dilatation of the urethra may occur. This may be brought about by means of a urethral calculus, urethral stricture, or traction on the urethra by scar tissue. The latter two conditions produce an increase in pressure behind the stricture on voiding.

The following congenital cysts may rupture into the urethra; Gärtner's duct cysts, cysts from faulty union of primal folds, probably as a result of the incomplete closure of the urogenital sinus (Carter, 1942), cell rests, Müllerian remnants and congenital dilatation of a paraurethral duct or gland (Huffman, 1948).

It may be very difficult to determine whether the aetiology is acquired or congenital or both. Where there is no history of trauma or infection, it is regarded by some as being congenital in origin. One would expect more cases if trauma is such an important aetiological factor. Most of the orifices of diverticula occur in the middle third of the urethra (Johnson, 1938), while the majority of the paraurethral duct orifices enter the distal third of the urethra and most of the glands are also related to this part of the urethra; this may cast a doubt on infection of the paraurethral glands as the sole cause. The intermittent filling and emptying of the cavity of a diverticulum may gradually cause an increase in its size. As the external urethral orifice is the narrowest and least distensible part of the urethra, there is back pressure with each voiding, causing an increase in the size of the diverticulum (Mayers, 1938; Furniss, 1935). Jarecki (1914–1917) reported a case in a virgin and Johnson (1938) a case in a child one day old. These 2 case reports favour a congenital origin. With engagement of the foetal head during labour, the urethra elongates and the bladder becomes almost entirely an abdominal organ (Kantor, 1950). If birth of the engaged foetal head is then delayed, some damage to the urethral muscularis may be brought about and this may be the initial stage in the development of a urethral diverticulum.

Some of the relevant points of the embryology, anatomy and histology of the urethra will be mentioned. Distal to the origin of the allantois from the primitive hindgut, the gut enlarges to form the cloaca. The cloaca is divided into two parts: a dorsal part which becomes the rectum and a ventral part which becomes the urogenital sinus by the downgrowth of the urorectal fold and a wedge-shaped mass of mesenchyme (Patten, 1952). The female urethra develops entirely from the original short neck between the bladder and urogenital sinus (Arey, 1946). The homologous part in the male is that part of the urethra extending from the bladder to the prostatic utricle (Huffman, 1948). The female urethra is of endodermal origin (Felix). The paraurethral glands arise above the Müllerian tubercle and first appear in the 50 mm. foetus as solid buds from the ventral and lateral sides of the urethra. The "glands" show branching in the 128 mm. foetus. The paraurethral glands are homologous with that portion of the prostate which is proximal to the prostatic utricle, developing above the union of the mesonephric ducts with the urogenital sinus (Huffman, 1948).

Embryologists have pointed out that the developmental history of the urethra provides abundant opportunity for the formation of diverticula (Wharton and Kearns, 1950).

The urethra is a hollow muscular organ made up of a mucosa, submucosa and a muscle layer. The mucous membrane is thrown into many longitudinal folds, with the result that the lumen is crescentic or stellate in shape on cross section (Krantz, 1951). The epithelium of the mucosa is stratified squamous in its anterior end, changing over to transitional in its posterior part (Mayers, 1938; Krantz, 1951). The submucosa is a loose connective tissue layer with an abundant elastic network and a highly developed venous plexus (Schmitz, 1939; Maximow and Bloom, 1946). This is surrounded by the muscularis, an inner smooth longitudinal and an outer smooth circular layer. When the longitudinal muscle layer contracts, the urethral lumen is widened while contraction of the circular layer has the opposite effect. In the proximal third of the urethra, these two layers are intermingled and the muscularis becomes an integral part of that of the bladder more proximally (Furniss, 1935; Krantz, 1951). In the region of the vesical neck there is no evidence of any hypertrophy or hyperplasia of the muscle layer suggesting a sphincter. Decussating striated muscle fibres from the bulbo- and ischiocavernosus muscles have a voluntary sphincteric action on the urethra. According to Krantz (1951) there are heavy fibrous bands of tissue extending from the lateral wall of the urethra, at the junction of the middle and upper thirds, to the pubic rami on each side, the so-called "puboprostatic ligaments" of the female urethra. In the submucosa and longitudinal muscle layers are to be found the paraurethral glands and ducts (Fig. 4), 6 to 31 in number according to Huffman (1948) in his series of dissections. These glands are branched tubular glands, lined by simple columnar epithelium. The ducts that enter near the meatus are lined with stratified squamous epithelium, those that open into the midurethra and proximal third are lined with the transitional type. The paraurethral glands are regarded as important in the production of abscesses and thus of subsequent diverticula (Huffman, 1948). De Graaf was probably the first to describe paraurethral ducts in the female (1672). These ducts have a tendency to run parallel to the urethra, especially in its distal third; but in addition the glands and ducts actually form a network around the urethra, the majority being around its distal third. There is, however, individual variation as far as the number and size of these glands is concerned. According to Huffman (1948) the majority of these ducts enter the urethra in its distal third, less in its middle third and only a few in its proximal third. Some of the ducts end in pockets or tiny dilated cystic spaces. Cystic dilatation of these ducts occurs commonly. Cabot and Shoemaker (1936) found a number of deep crypts and invaginations of the mucosa along the female urethra and stated that these crypts could easily be mistaken for paraurethral glands. The paraurethral glands have a slight secretory activity (Huffman, 1948). There is, however, no unanimity of opinion regarding the presence of glands around the urethra. Obstruction of the narrow outlet of infected ducts is possibly a factor in the aetiology of abscesses of the anterior vaginal wall (Huffman, 1948).

The average length of the urethra is 35 mm. (Mayers, 1938). The urethra is narrowest and least distensible at the external meatus and this may be an important factor in increasing the intraurethral pressure during micturition, thus emphasizing any latent weakness in the urethra (Furniss, 1935). Nordenström (1952) describes the female urethra as having two angulations, dividing it into posterior, middle and anterior parts. The middle section is the common site for a diverticulum. The lower two thirds of the urethra are inseparable from the anterior vaginal wall, forming an integral part of this structure, because of decussation of vaginal muscle fibres around the urethra (Krantz, 1951). This may be a reason why this site may be more readily traumatized.

The *pathology* of urethral diverticulum has been described by various authors (Counseller, 1949; Downer and Virgilo, 1945; Engel, 1941; Everett, 1947; Folsom and O'Brien, 1945; Heaney, 1949; Herman and Greene, 1944; Higgins and Rambousck, 1945; Johnson, 1938; McNally, 1935; McMahon, 1946; Parmenter, 1941; Schmitz, 1939; Schmitz and Nelson, 1939).

In some cases the wall is thick and fibrous and dissection is relatively easy, while in others the wall is thin and friable so that dissection in one piece is difficult. The sac may have all the layers of the urethral wall or may show a break in the continuity of the muscular layer or of all the layers of the urethral wall. The urine in the sac is very often infected and the majority of cases show chronic inflammation in the wall. The lining membrane of the sac may show squamous, columnar, cuboidal, transitional or stratified squamous epithelium, or a lining membrane may be absent, the inner surface consisting of granulation and fibrous tissue, as is usual with infection and abscess formation. Glandular tissue may be found in the sac wall.

Symptoms: (Table IV). (Counseller, 1949; Everett, 1947; Higgins and Rambousck, 1945; Johnson, 1938; Heaney, 1949; Herman and Greene, 1944; Folsom and O'Brien, 1945; Pratt, 1938; Wharton and Kearns, 1950; Schmitz, 1939.)

The condition may be symptomless, particularly if small and uninfected. Pain may be located over the lower abdominal, suprapubic or perineal regions. A sensation of pressure or weight in the vagina or actual pain may be suffered. The pain may radiate upwards from the urethra to the pelvic organs. An associated backache is often present. The pain may be accentuated in the sitting position.

Apart from dysuria and frequency, the patient often gives a history of recurrent "cystitis" or treatment of so-called "cystitis" without cure. Post-micturitional dribbling is a symptom found in very few other conditions. Dyspareunia is frequently present and obviously is mechanical in origin and therefore is worse should complications be present.

The patient may complain of a vaginal mass and may volunteer that digital pressure causes a gush of urine. Apart from these common symptoms, the patient may occasionally complain of haematuria. This may be terminal. There may be a sudden discharge of pus through the urethra, followed by relief of symptoms. After voiding, the patient may have the feeling that the bladder is not quite empty.

There may be a history of chills and fever, depending on the extent of the superadded infection. The symptoms may date from the time of a confinement.

Signs and Special Investigations: (Counseller, 1949; Everett, 1947; Higgins and Rambousck, 1945; Johnson, 1938; Menville and Mitchell, 1944; Schmitz, 1939; Townsend, 1938; Wharton and Kearns, 1950).

A mass is the most important single sign. It is situated in the anterior vaginal wall. The average size is 2–3 cm. in diameter. It may be tender and/or indurated, depending upon the degree of infection. It may fluctuate. Digital pressure may cause urine or pus to escape from the urethral orifice. The urine may be foul smelling. The common site is the middle third of the urethra, but it must not be forgotten that the diverticulum may track as far as the trigone. A sound may be made to enter the pouch.

Examination of voided urine reveals pus, which is not present in a catheter specimen. The opening in the urethra may be demonstrated by urethroscopic examination; it may, however, be necessary to repeat this investigation as a small opening may be missed.

TABLE IV

Symptoms—Common	Symptoms—Uncommon
1. Pain: (a) Low abdominal	1. Haematuria.
(b) Perineal.	2. Sudden discharge with relief.
(c) Vaginal.	3. After voiding, bladder not empty.
(d) Urethral—pelvic organs.	
(e) Backache.	
2. Dysuria and frequency—recurrent cystitis.	
3. Post micturitional dribbling.	
4. Dyspareunia.	
5. Vaginal mass.	

Visualization by radiography is rather difficult, because of the difficulty in retaining the contrasting medium in the urethra. The following radiographic methods have been recommended: (*a*) Coiling a urethral catheter in the sac; (*b*) filling the bladder with an opaque medium and making the patient strain against resistance and filling the sac with an opaque jelly as recommended by Townsend (1938). Radiography will demonstrate the site and extent of the diverticulum.

The *differential diagnosis* presents very few difficulties. Diverticulum of the urethra has to be distinguished from only a few conditions.

Infected paraurethral glands can be excluded by the absence of a pouch; induration and tenderness are, however, present in both conditions. Chronic urethritis is distinguished by the absence of a pouch and by urethroscopic investigation. No sac, separate from the urethra, will be found in the case of a urethrocoele; usually there is an associated cystocoele. Embryological remnants can be excluded by the absence of post-micturitional dribbling and palpation. There should be no difficulty in the diagnosis of suburethral folds following colporrhaphy. Epithelioma of a paraurethral gland is extremely rare and its consistency is firm. The diagnosis is easily made, should the condition be borne in mind. Because of the tendency of periodic emptying, the diverticulum may readily be missed. The patient should be examined immediately after micturition. Repeated treatment for so-called recurrent attacks of "cystitis" should put the examiner on his guard. Therefore the urethra must be examined and palpated in its entire length in cases of repeated attacks of lower urinary infections. Richard Cabot (quoted by Folsom and O'Brien, 1945) remarked that the female urethra should be suspected in the case of pain (situated within two feet of its orifice) for which an adequate explanation is lacking. The diagnosis can be made without visual intraurethral examination.

Complications. Infection is present in the majority of cases and this may go on to abscess formation. Infection is especially liable to supervene should there be incomplete emptying of the diverticulum (Counseller, 1949; Menville and Mitchell, 1944; Wharton and Kearns, 1950).

Calculus formation may be the cause or complication of a diverticulum. According to Herman and Greene (1944) the composition of the stone is chiefly ammonium phosphate. Prior to 1949, 44 such complications were reported in the literature. The development of calculus depends upon urinary stasis and infection (Hunner, 1938; Kirby and Reynolds, 1949; McMahon, 1946; Menville and Mitchell, 1944; Shivers and Cooney, 1934). Wharton and Kearns (1950) described a case of arthritis that disappeared following excision of a diverticulum of the urethra.

One case with epitheliomatous change has been reported by Walters and Thiessen (quoted by Menville and Mitchell, 1944). A diverticulum may be the cause of urethral haemorrhage (Menville and Mitchell, 1944). Fistula and stricture may follow operation if due care is not exercised.

Treatment. Complete excision of the diverticulum and repair of the urethra should be carried out except in cases of abscess formation, where only incision is advised (Counseller, 1949). At the operation preliminary dilatation of the urethra is carried out to a degree which can comfortably be accommodated. The dilator is left in for the duration of the operation. The anterior vaginal wall is incised in the midline. The sac is carefully dissected out and severed from the urethra. The defect in the urethral mucosa is closed with a purse-string suture. The suburethral tissues are brought together with interrupted sutures. The redundant vaginal mucosa is trimmed away from only one side, so that the flap from the opposite side may be brought across the midline. A self-retaining catheter is left in for 4 days, in order to drain the bladder and splint the urethra. Gauze is introduced to exert pressure beneath the urethra, preventing potential dead space. The plug is removed 48 hours later. The patient should be up on the fourth day. Preliminary suprapubic drainage is regarded as too radical a procedure (Everett, 1947; Furniss, 1935; Hunner, 1938; Hyams and Hyams, 1939; Menville and Mitchell, 1944; Schmitz, 1939; Wharton and Kearns, 1950).

Moore (1952) advises that through a small stab wound in the diverticulum a Foley's catheter be

inserted; the distended Foley's bag permits traction and thus easy dissection. Should the sac be very friable and adherent to the bladder, as much of it as possible should be excised and the lining destroyed with carbolic acid; a catheter is then left in for 10 days. Suprapubic drainage may be considered in the presence of a large stone (Shivers and Cooney, 1934). Should the patient refuse operation, or if an operation is contra-indicated, periodic dilatation of the urethra and urethral irrigation with antiseptics are advised. Other procedures, e.g., electro-coagulation, have been abandoned in favour of radical removal of the sac as advocated by Hunner (1938). Post-operative fistulae usually heal spontaneously. Patients with minor diverticula often do not even seek professional assistance.

Case Report

From July, 1948 to June, 1953, 9,815 patients were admitted to the Groote Schuur Gynaecological Wards for operation. One patient only was admitted diagnosed as suffering from a diverticulum of the urethra.

A 32-year-old coloured woman was admitted on 10th April, 1953, for stress incontinence. Her urinary complaint dated from the birth of her third child in 1948, i.e., following upon the instrumental delivery of a still-born child. Frequency and dysuria were the prominent symptoms. The so-called stress incontinence actually was post-micturitional dribbling. This very nervous patient also complained of dyspareunia, low backache and tenderness in her vagina. Vaginal examination (Fig. 5) revealed a slightly deficient perineum and a patulous urethral meatus. On the anterior vaginal wall was a tender, soft, fluctuating mass 2 cm. in diameter and overlying the distal third of the urethra.

Examination immediately after micturition revealed dribbling on coughing. Pressure on the mass produced the same effect. A metal catheter could be inserted into the pouch.

The operation was done along the lines described by Hunner (1938). The urethra was not dilated, as the external meatus was patulous. The vagina was not packed, as no dead space was left. The perineum was also repaired.

The patient made an uneventful recovery. She was free of symptoms and signs 2 and 4 months post-operatively.

As the female urethra is the connecting link between the domains of the gynaecologist and the urologist, it may be just the site that is neglected by both specialities. Gynaecologists should milk and palpate the urethra whenever a gynaecological examination is undertaken. Alert consideration will prevent misdiagnosis.

Summary

The clinical features and treatment of diverticulum of the female urethra are discussed and the pertinent literature is reviewed. The case history of a patient admitted to the Groote Schuur Hospital is presented.

I wish to express my appreciation to Professor J. T. Louw for his encouragement and helpful criticism.

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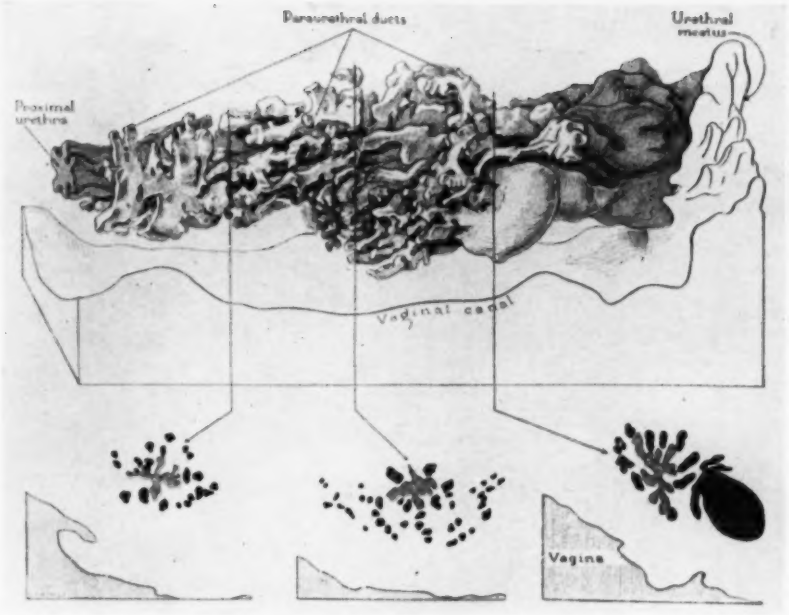

FIG. 4

Paraurethral Glands surrounding the Urethra.

Drawing of wax model of an adult human female urethra with its paraurethral ducts and glands as seen in right lateral view. This reconstruction is in reality a cast of the urethral canal with its outpouching ducts and glandular pockets. The base of the model labelled "Vaginal canal" represents a cast of that portion of the vagina which is beneath and parallel to the urethra. The smaller diagrams demonstrate transverse sections through the urethra, the paraurethral ducts and glands and the vaginal canal beneath the urethra at different levels above the meatus. Tissues from which this model was reconstructed were obtained at necropsy of a 20-year-old virgin. This model represents the distal 2·4 cm. of a urethra which had a total length of 2·8 cm. It will be noted that no paraurethral ducts open at or immediately within the urethral meatus. Thirty-one ducts empty into this urethra. Although most of these ducts empty into the distal third of the urethra, several others empty into the middle and proximal thirds. After leaving the urethra the ducts turn cephalad and extend parallel with the urethral canal. One large duct on the right develops into a cyst of considerable size. At the midpoint in the urethra many ducts and glands extend laterally far from the canal; at a more proximal level the urethra is surrounded by many small tubules, and on the right it is encompassed by a thin compact semi-circular sheet of ducts and glands.

(With kind permission of John W. Huffman and the *American Journal of Obstetrics and Gynecology*, 1948, **55**, 89.)

FIG. 5

Urethral diverticulum causing a swelling on the anterior vaginal wall.

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LOWER NEPHRON NEPHROSIS IN THE NEWBORN

BY

I. KESSEL, M.B., M.R.C.P.(Lond. and Edin.), D.C.H.

Department of Paediatrics, University of the Witwatersrand, and the Transvaal Memorial Hospital for Children, Johannesburg

AND

W. J. PEPLER, B.Sc., M.B.

South African Institute for Medical Research, Johannesburg, South Africa

IN 1941 Bywaters and Beall recorded the occurrence of lower nephron nephrosis following crush injuries. Lucké (1946) recorded the renal lesions of the crush syndrome, and also that of burns, transfusions and other conditions affecting the lower segment of nephrons. The study of this disease has received a great deal of attention, and many reports of similar renal changes have been recorded in a wide variety of conditions, such as incompatible blood transfusions, crush injuries, shock, reaction to sulphonamides, placental haemorrhages, burns and many other affections. The conditions are all characterized by shock or intravascular haemolysis or both. At autopsy one usually finds enlarged kidneys with pallor of the cortex and congestion of the medulla, with histological evidence of tubular degeneration; these changes are believed by some pathologists to be limited to the distal tubules, whereas others such as Moon (1950) maintain that the proximal tubules are equally affected. Phillips *et al.* (1946) have noted the susceptibility of the renal circulation to shock, and Jonsson (1951) maintains that anoxia, due to some disturbance in renal circulation, is the main factor in causing the renal changes. Jonsson has recorded 3 cases of lower nephron nephrosis associated with severe neonatal asphyxia. They all developed signs of renal insufficiency during the first week of life, with a rise in non-protein nitrogen of 90-127 mg. per cent. Two of Jonsson's cases had oliguria and 1 died; an autopsy of this case showed capillary damage with perivascular haemorrhages in different organs, as found in cases of asphyxia. Jonsson discusses the respiratory insufficiency associated with circulatory collapse and shock found in asphyxia neonatorum; all his 3 cases had pronounced shock symptoms. The cause of the neonatal asphyxia may be variable. The asphyxia in 2 of Jonsson's cases was due to intracranial damage and in the third to atelectasis with poor respiratory function.

These renal lesions have not been recorded in the newborn with the exception of Jonsson's cases, and the reason may be, as he suggests, that one fails to look for the condition. However, very severe anoxia must be necessary to produce the lesions, and we wish to record a further case of lower nephron nephrosis in a newborn full-time female infant.

CASE REPORT

Mrs. B., aged 26 years, gave birth to her second child in December, 1952. Her first, a boy, weighing 8¼ pounds at birth, was normal.

During her second pregnancy she became very oedematous, but her blood pressure remained normal. The first stage of labour lasted 5½ hours and the second stage 25 minutes. Her membranes were artificially ruptured and meconium-stained liquor drained away. The foetal heart was irregular at a rate of 150 per minute. She was delivered of a full-time live female child weighing 7 pounds 15¾ ounces and measuring 21 inches in length. Much meconium-stained mucus was sucked from the infant's mouth and air passages, and oxygen and stimulants were administered. The child died 30 minutes after birth. The placenta was of the discoid type and weighed 2 pounds 1 ounce. The cord was 32 inches long and was inserted laterally in the placenta.

Autopsy

The body was that of a full-time European female infant weighing 7 pounds 15¾ ounces and measuring

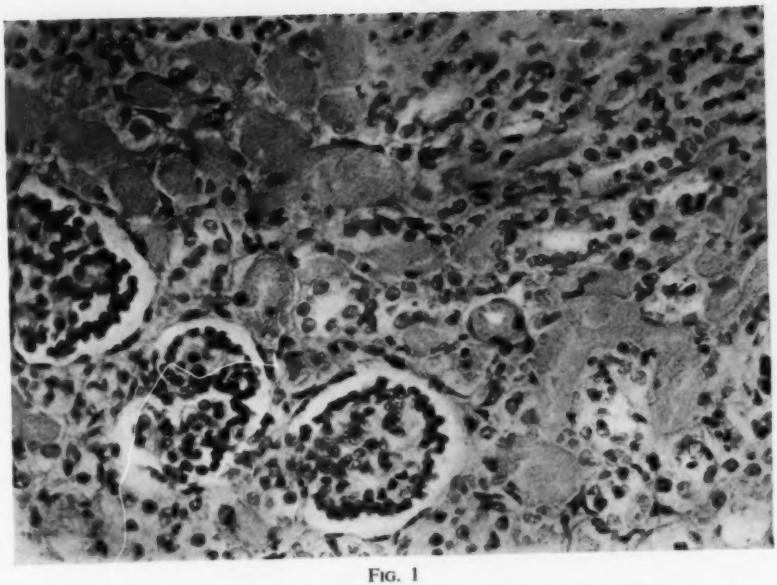

FIG. 1

Lower nephron nephrosis showing tubular degeneration. ×315.

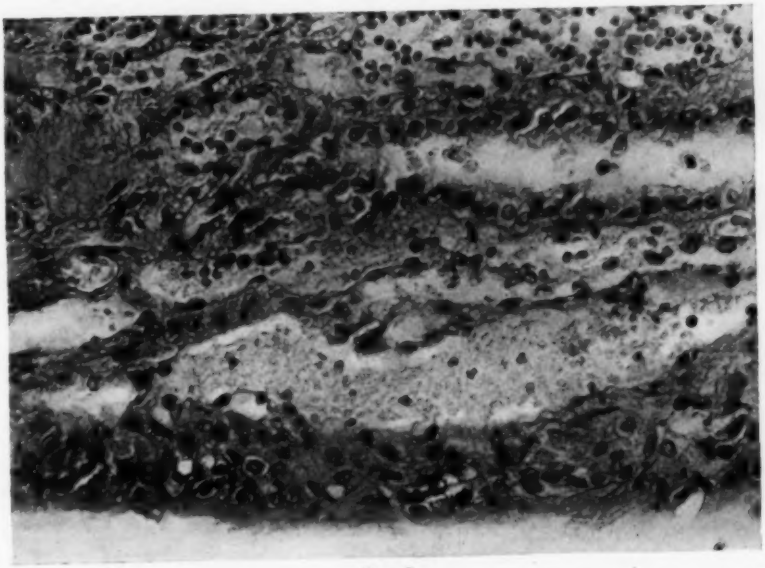

FIG. 2

Lower nephron nephrosis showing granular cast in collecting tubule. ×315.

21 inches in length. There was no external evidence of oedema, jaundice or trauma. The respiratory passages were filled with meconium-stained material. The lungs showed many subpleural petechial haemorrhages and were fairly well-aerated except for patchy atelectatic foci. The heart showed many subepicardial haemorrhages. The brain was congested and oedematous, but there were no haemorrhages. The kidneys were enlarged and on section showed an intensely congested medulla, with a pale cortex.

Histological Examination

Histological sections taken from the left ventricular myocardium, the thyroid gland, brain, pancreas and suprarenal gland revealed no significant pathological change. The liver on histological section showed well-marked congestion and dilatation of the sinusoids. The spleen and thymus on histological section showed the presence of congestion only. Section of the specimen from the lung showed the presence of congestion of the alveolar capillaries, and extravasation of oedema fluid and an occasional red blood cell into some of the alveoli. The bronchi appeared healthy.

Microscopic examination of the kidney showed the presence of normal glomeruli. The most conspicuous feature was the degeneration of the epithelium of the distal convoluted tubules (Fig. 1) but the epithelial linings of the proximal convoluted tubules were intact. The collecting tubules contained brownish-red granular haemoglobin casts (Fig. 2). The interstitial tissue of the medulla was intensely congested.

Discussion

This infant, a full-time female, suffered intra-uterine anoxia as evidenced by the meconium-stained liquor amnii, the irregular foetal heart rhythm and the subepicardial and subpleural petechial haemorrhages, as well as the congestion of organs on histological examination. She survived for 30 minutes after birth and autopsy revealed the effects of the asphyxia and evidence of a lower nephron nephrosis. The treatment of such conditions must be that of the management of the asphyxial states of the newborn with the provision of oxygen and other necessary measures. Dausset (1950) has treated cases of lower nephron nephrosis with repeated exchange transfusions.

Summary

A case of lower nephron nephrosis in a full-time European female infant is recorded. This child died 30 minutes after birth. The association of this renal condition with severe neonatal asphyxia is discussed and the literature is briefly reviewed.

We wish to thank Prof. O. S. Heyns and Dr. L. Van Dongen for referring this case to us and for permission to publish it.

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LEUKAEMIA WITH PRIMARY GYNAECOLOGICAL MANIFESTATIONS

Record of a Case and Review of Literature

BY

S. A. GUEUKDJIAN, M.D.

King Edward Memorial Hospital, London

LEUKAEMIA is a general disorder of the blood and it is possible to have leukaemic infiltration of any tissue in the body. Primary manifestations outside the usual organs, however, may easily escape notice on routine examination.

Thus, although in obstetrics leukaemia has been quite often associated with ante-partum haemorrhage, in gynaecology the disease seems to be a rare occurrence as a primary manifestation. There are only a few recorded cases of leukaemia starting with gynaecological symptoms and the following case seems worthy of mention.

CASE REPORT

A woman of 76 was seen at the gynaecological outpatient department for the investigation of pain and bleeding *per vaginam*. She stated that she had normally enjoyed good health, had had 3 uneventful pregnancies and at 53 had a normal menopause. Since then she had never lost any blood until this year. For the past 10 months she had intermittent vaginal bleeding and recently she also had pain in the vulva. She had lost no weight and in general felt well. She also incidentally mentioned that for the past 6 years she had noticed some lumps in the groins but never paid any attention to them.

On examination the patient seemed in good health and well preserved for her age. The heart, chest and abdomen were normal. She had moderately enlarged inguinal glands. The uterus and adnexa felt normal while the cervix looked unhealthy and easily bled to touch. There was also a urethral caruncle of considerable size. Her haemoglobin was 13·3 g. per 100 ml. (90 per cent).

She was admitted to the ward and on 16th August, 1953 operation was performed with diathermy-excision of the urethral caruncle. Examination under anaesthesia revealed a small, mobile, normal uterus and atrophic appendages. The cervix was ulcerated and bled easily to touch. Curettage was performed and a cervical biopsy taken, the site being sutured with two haemostatic stitches.

The patient was making normal progress when, 9 days later, she had a secondary haemorrhage *per vaginam*, necessitating re-examination under anaesthesia. The caruncle site had healed; the biopsy sutures seemed intact but there was a general ooze from the cervix, impossible to arrest by ligation. Haemostasis was effected by vaginal packing, and a blood transfusion of 2 pints given as her haemoglobin had dropped from 91 to 66 per cent. The full blood count was as follows: haemoglobin 66 per cent; red cells 3,000,000 per c.mm.; colour index 1·1; size 6·8 microns; white cells 56,000 per c.mm., of which 87·5 per cent were lymphocytes, 11·5 per cent polymorphs and 1·0 per cent monocytes; platelets 160,000 per c.mm., numerous smudge cells; bleeding time 1½ minutes. The diagnosis of lymphatic leukaemia was made, and this was further strengthened by the clinical findings of a discrete adenopathy and a palpable spleen, with a negative Paul Bunnell test. Histology of the uterine sections revealed lymphocytic infiltration of the cervix and endometrium.

Specific treatment for the leukaemia was not considered necessary as the patient's immediate condition improved satisfactorily. When last seen as an outpatient she felt well and had had no further bleeding. Her blood picture was: haemoglobin 95 per cent, white cells 55,400 per c.mm., lymphocytes 94·5 per cent, monocytes 1·0 per cent, polymorphs 4·5 per cent, smudge cells present.

COMMENT

Leukaemia as a cause of uterine bleeding is only hinted at *en passant* in most standard works of haematology and gynaecology, while many textbooks do not even mention it. Where mention is made, there is no differentiation between bleeding due to platelet deficiency and bleeding due to actual infiltration of the cervix or endometrium. Moore White (1944) says that "uterine haemorrhage may be a symptom of most of the blood diseases". Browne (1950) states that "such blood diseases as splenic anaemia, idiopathic hypochromic anaemia, aplastic anaemia, leukaemias and thrombocytopoenic purpuras may be associated with menorrhagia". From these

FIG. 1

Superficial ulceration of the cervix with leukocytic infiltration. Haematoxylin and eosin. ×160.

FIG. 2

Perivascular lymphocytic infiltration of the cervix. Haematoxylin and eosin. ×170.

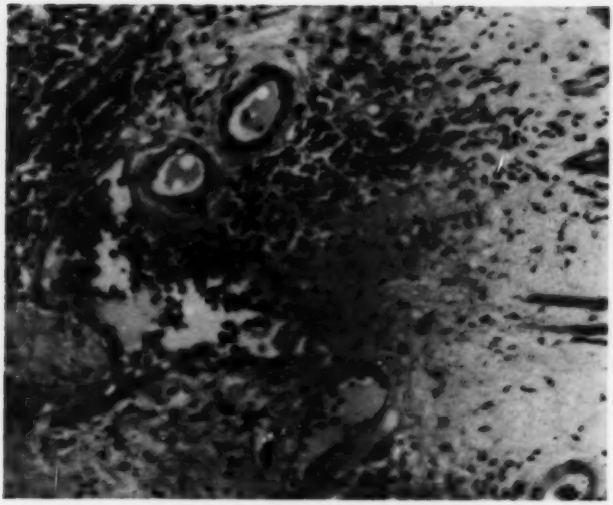

FIG. 3

Leukaemic infiltration with margination of lymphocytes in small vessels. Haematoxylin and eosin. ×210.

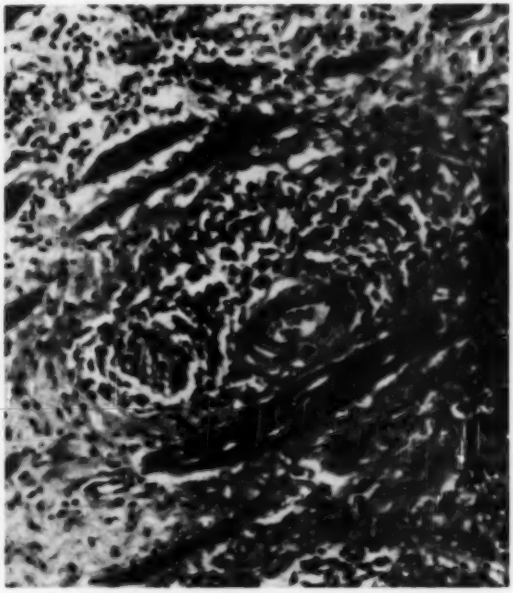

FIG. 4

Lymphocytic invasion of the cervix with perivascular infiltration and "cuffing". Haematoxylin and eosin. ×380.

observations we are given to understand that in leukaemia the uterus, together with other organs, may be the site of bleeding. Primary gynaecological manifestations are not mentioned. Shaw (1949) points out that "in chronic blood diseases pure menorrhagia is an infrequent symptom, although irregular and continuous bleeding sometimes develops in severe cases". In Jones and Cantor's (1951) 10-year survey of post-menopausal bleeding leukaemia is not even hinted at as a possible cause of metrorrhagia.

In obstetrics leukaemic complications are not so uncommon, and Slentz (1951) has been able to collect a total number of 106 cases on record up to that year. However leukaemia with primary gynaecological manifestations remains an extremely rare occurrence, and including ours we cannot find more than 5 cases on record.

Wheaton (1952) in this country and Berwind (1952) in Germany first drew attention to this condition less than 2 years ago. Wheaton's report consists of 3 cases of leukaemia in women who came with severe uterine bleeding. In all 3 the type of leukaemia was myeloblastic, and this is curious, for Whitby and Britton (1950) say that "in myelocytic leukaemia the female reproductive system shows infiltration of the organs with myeloid cells but amenorrhoea or scanty menstruation is common". Yet all 3 patients died of leukaemic hypermenorrhoea. It is unfortunate that in this list no mention is made as to whether there was actual myeloid infiltration of the uterus.

Berwind's patient was a woman of 76 whose main complaint was post-menopausal bleeding. The blood picture showed typical leukaemia and biopsy revealed actual lymphocytic infiltration of the uterus.

Our case also was one of lymphatic leukaemia which appeared under identical conditions of post-menopausal metrorrhagia in a woman of 76. Besides these 2 cases we can find no other record of lymphatic leukaemia with primary gynaecological manifestations. Though Beckwith Whitehouse (1935) briefly mentions another "case of fatal menstrual haemorrhage in a patient suffering from lymphatic leukaemia", there is no mention whether menorrhagia was the first sign of her disease, and the 3 cases that Dr. Neumark (1953) kindly communicated to us had some other gynaecological pathology besides the leukaemic infiltration of the uterus. Our histological findings (see photomicrographs) are evidence that the bleeding was due not merely to a low platelet count (this, in fact, was not very low in our patient) but due to actual leukaemic infiltration of the uterus.

Summary

A rare case of lymphatic leukaemia presenting as post-menopausal bleeding is reported, and the literature on the problem is reviewed.

I would like to record my thanks to Miss A. M. Dickins for her advice and permission to treat and publish this case, to Dr. W. S. Killpack for the pathological reports and to Dr. E. Neumark for the photomicrographs.

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APPROACH TO THE DELIVERY OF THE HYPEREXTENDED FOETUS

BY

GERALD J. AMIEL, M.B., M.R.C.O.G.

Obstetrician and Gynaecologist

Bromley Group of Hospitals, Kent

MARKED hyperextension of a foetus *in utero* is a comparatively rare condition and when encountered the decision as to the best mode of delivery may present considerable difficulty. Kobak (1946) and Deacon (1951) both point out the paucity of references to the condition in the literature, and describe their cases in which delivery was by Caesarean section. Deacon's case was however complicated by a pelvic outlet contraction. This paper presents a case report in which spontaneous birth occurred where operative delivery had been planned. The case prompted a study of the available literature and has led to some observations concerning the delivery of the hyperextended foetus.

It would seem that whatever the foetal lie, when hyperextension is present, dystocia may ensue. Falls (1917), Burns (1928), Knowlton (1938), Nagyfy (1949) and Denny (1951) all described cases in which the hyperextension was associated with a transverse lie. Successful external cephalic version was found to be impossible, and in 4 of the 5 cases Caesarean section produced a living child. In the fifth, that of Falls, extraction of the foetus at 3-fingers dilatation done "in the interest of the child" produced a baby which failed to survive.

Where the condition, which American writers prefer to call "opisthotonus foetalis" after Falls, is associated with a persistent transverse lie (the term "flying foetus" was introduced by Knowlton) there is undoubtedly a very strong case for delivery by Caesarean section. It is in those cases where there is persistent hyperextension in association with a longitudinal lie that the question of delivery *per vias naturales* gives rise to some concern. The problem is illustrated by the following example.

CASE REPORT

The patient, a healthy woman of 24, was first examined at Beckenham Maternity Hospital on 6th August, 1952 when 12-weeks pregnant. One previous pregnancy in 1951 had resulted in the spontaneous delivery of a healthy male infant weighing 6 pounds 13 ounces. Examination revealed no abnormality, and the estimated date of delivery was calculated as 19th February, 1953. The pregnancy progressed normally until the patient was referred to the writer on 9th January, 1953 on account of a breech presentation. She was then 34-weeks pregnant and the position was diagnosed as left sacro-anterior. The breech was not engaged yet attempted external cephalic version was unsuccessful. A further attempt in an anticlockwise direction 7 days later also failed.

X-ray examination on 21st January, 1953 showed the attitude of the foetus to be grossly abnormal (Fig. 1). Extension of the head was associated with acute hyperextension of the spine from and above the level of approximately the first thoracic vertebra. The foetal abdomen was facing forwards and upwards and one arm appeared to be extended behind the head. The radiologist's report ended with the query "Are foetal heart sounds heard?"

On 23rd January, 1953, further external cephalic version was attempted without avail and 3 days later the X-rays were repeated (Fig. 2). The gross hyperextension of the spine was again clearly demonstrated although the attitude of the limbs had altered. The radiologist reported thus: "The re-examination again shows the hyperextension of the foetal spine in the region of T1. This cannot be artefact and since it is difficult to imagine anything outside the foetus which would cause this attitude, I think this must be regarded as a foetal abnormality ? inioncephaly."

On 30th January, 1953 the position seemed little changed although the head was to the left of the midline. Version in the shorter clockwise direction was successful with surprisingly little difficulty. The foetal heart remained satisfactory. An abdominal binder with pads was placed in position. X-ray was repeated the same day (Fig. 3) and showed that the version had not altered the hyperextension of the spine. The faulty attitude was still palpable clinically on 4th February, 1953 when the presentation was considered to be either a brow or face. The head could not be made to engage in the pelvis.

FIG. 1

Lateral X-ray view (21st January, 1953) shows the acute hyperextension of the cervical spine.

FIG. 2

Antero-posterior view (26th January, 1953).

FIG. 3

External cephalic version has succeeded but cervical spine remains hyperextended. X-ray taken 30th January, 1953.

FIG. 4

X-ray of the 3-day-old baby demonstrates the tendency to hold the neck extended.

The management of the case was discussed with Mr. Douglas Lindsay. He recalled one of his cases several years previously where vaginal delivery had been attempted under not dissimilar circumstances, and inioncephaly associated with other congenital abnormalities had resulted in a very difficult extraction necessitating perforation and craniotomy. The mother at the time had suffered considerable shock. After consideration of all circumstances we decided therefore that elective Caesarean section would be the safest mode of delivery even though a normal foetus was considered to be an unlikely outcome. Before this operation could be carried out, however, labour commenced spontaneously. When seen shortly after this, the head was deeply engaged and strong contractions were occurring every few minutes. Within a very short time the membranes ruptured and concurrently full dilatation was reached. Within 5 minutes the vertex was visible and an easy spontaneous delivery occurred. The total duration of labour was 2 hours 25 minutes, the 1st stage lasting 2 hours and the 2nd and 3rd stages 15 and 10 minutes respectively.

The male infant, weighing 7 pounds 3 ounces, appeared normal except that it lay with its head obviously hyperextended for the first 3 days (Fig. 4). This attitude was still noticed after 7 days but appeared to be diminishing. Subsequent progress was quite normal. The infant was thrice examined in conjunction with the Paediatrician when aged 5 weeks, 4 months and 1 year. At 5 weeks the child seemed to prefer to hold his head back, but full flexion was not resented. This, according to the mother, persisted for 2½ months. When 4 months old, the baby was apparently normal and he was developing satisfactorily at 1 year.

Radiological examination of the skeletal structure showed the presence of a spina bifida of the atlas. The condition was without symptoms, and, had not full X-ray examination been repeated, this spina bifida occulta would not have been discovered. There was certainly no other detectable abnormality on careful examination of the infant. Maternal progress following delivery was normal.

Comment and Discussion

The persistence of the hyperextended attitude of the foetus *in utero* before and after version, and in the infant for some weeks after delivery, has been noted by other writers. Gibberd (1935) mentions a case delivered by Caesarean section in which superextension of the spine was maintained over 5 days in spite of alteration of the lie from longitudinal to oblique. In Denny's case (1951) hyperextension persisted for 6 weeks and according to the mother there was a tendency for the child to throw its head right back for 7 months. Wilkin (1951) reported a primary face presentation with spontaneous delivery after successful external version of a hyperextended breech. The attitude was maintained for the first 3–4 days of life.

The aetiology of the hyperextension is a matter of conjecture, but I attribute it, accepting the views of Gibberd (1939), to excessive tone in the extensor muscles. It seems reasonable therefore, to suppose that, in the case here reported, the forces of labour overcame the muscular imbalance, and head and spine flexed while normal delivery proceeded. Natural forces unaided, apparently corrected the malposition without much difficulty, yet as soon as the baby was delivered, the attitude of hyperextension was resumed though in a lesser degree. One naturally considered the possibility of some connexion between the spina bifida of the atlas and the abnormal foetal attitude, but after full discussion with several colleagues no connexion could be suggested, and I am inclined to regard this finding as coincidental.

The unpredicted outcome of this case led to the conclusion that, where doubt as to the mode of delivery existed, a "trial of labour" might provide the answer to the problem. As for a trial in a case of possible disproportion one essential must be that the head presents. In examining the literature with regard to mode of delivery in hyperextended attitudes associated with longitudinal lies, one finds some conflict of opinion as far as breech presentations are concerned.

Hall (1952) reported 2 cases of breech presentation followed by spontaneous delivery. Melody (1948) contemplated Caesarean section, but, after repeated X-ray had shown the spontaneous disappearance of the hyperextended state, a normal breech delivery ensued. Gibberd (1935) had previously reported a case in which spontaneous version had occurred with a disappearance of hyperextension. Taylor (1948) and Dougherty *et al.* (1953) both resorted to Caesarean section to deliver breeches with hyperextension of the neck.

In a review of the results of breech delivery in New York Hospital from 1932–1947, where a radiological survey of 216 breech presentations had been made, Wilcox (1949) found that hyperextension of the spine occurred only where hyperextension of the vertex was present. In 11 such cases there were 6 breech extractions (1 baby suffered from aphasia and paralysis), 3

spontaneous deliveries and 2 Caesarean sections. However, of the only 2 cases of marked hyperextension which were published with full details and X-rays, one was delivered by Caesarean section and the other was extracted, forceps being applied to the aftercoming head. This infant was later found to have a transection of the cord at the level of the first thoracic vertebra which Wilcox considered might possibly have been caused by pressure *in utero*. He states "we do not believe Caesarean section is indicated because of a hyperextended vertex per se. Individualization of such cases must be stressed."

Taylor's breech (1948) although delivered by Caesarean section was found to have a forward dislocation of the first 3 cervical vertebrae upon the fourth, which he considered to be intra-uterine in origin because of the ease of delivery and the fact that no attempts at version had been made. He concludes by saying that it is "reasonable to suppose that labour in the presence of hyperextension of the cervical spine could cause fatal damage to the cord". Dougherty *et al.* (1953) state that, where breech with a hyperextended head is diagnosed, treatment is by "external manipulation looking toward flexing it, or, failing this simple procedure, Caesarean section". Most will agree with this statement as it does appear likely that there is an added risk to the foetus if it is delivered as a breech in the hyperextended attitude. On the other hand, both of Hall's cases (1952) resulted in spontaneous delivery, hyperextension of the cervical spine being overcome during the second stage of labour. In spite of this, one cannot but feel that there must be considerable added concern during a breech delivery associated with hyperextension.

It would thus seem profitable to make the problem of delivery less complicated by attempting to make a cephalic presentation. Labour may then be given a trial in order to determine whether or not natural forces will overcome the muscular imbalance of the foetus. The case described pointed to the fact that perseverance in attempting external cephalic version was justified. Stein (1941) states external cephalic version is "contraindicated in the presence of deflexion as manipulation may increase deflexion". Vartan (1945), however, says "there is no need to fear causing the extended attitude; that is there already". Version in the case here reported had been attempted in the usual accepted direction and failed, and when the procedure was reversed success was easily achieved. This may well have been coincidence, as one often finds the manœuvre succeeds where previous attempts had failed, but version in the clockwise direction could certainly not be said here to have been aimed at flexing the foetus. The point of view taken was in line with that expressed by Vartan, and the patient was not subjected to Caesarean section which events showed would have been unnecessary.

Approach to Mode of Delivery

The problem therefore of the mode of delivery in the hyperextended foetus seemed to crystallize in the following manner. Caesarean section is undoubtedly the method of choice where the lie is persistently transverse or oblique. In breech presentations where there is added risk to the foetus, even when flexed, the additional complicating feature of hyperextension makes the risk of vaginal delivery considerable. Thus X-ray examination should be taken as soon as labour is established to ascertain if spontaneous flexion has occurred, and, if not, Caesarean section is desirable. Efforts should be made, however, to turn the breech into a cephalic presentation, when either a spontaneous face delivery may occur, or a "trial of labour" may be undertaken to see whether the forces of labour themselves may overcome the hyperextension. Only after failure of such a trial should Caesarean section be performed.

Summary

A case is described where a persistent hyperextended attitude in a foetus was overcome by the forces of labour and allowed of a spontaneous vertex delivery. The finding of a spina bifida of the atlas is reported. Other cases in the literature are briefly reviewed, and conclusions as to a method of approach to the problem of delivery of the hyperextended foetus are drawn.

I wish to express my thanks to Mr. Douglas Lindsay, Director of the Obstetric and Gynaecological Unit, for much helpful advice, and to Dr. S. D. V. Weller, Consultant Paediatrician

and Dr. A. C. Glendinning, Consultant Radiologist, for their co-operation.

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A CASE OF POST-PARTUM TUBERCULOUS ENDOMETRITIS

BY

R. A. McINROY, B.Sc., M.B., D.T.M. & H.

AND

G. A. CRAIG, *M.B.E.*, F.R.C.S.E., M.R.C.O.G.

Department of Pathology, St. Luke's Hospital, Bradford

THIS report describes an incomplete abortion which failed to respond to therapeutic curettage. Subsequent diagnostic curettage, with histological examination of the curettings, confirmed pregnancy and revealed tuberculosis involving both endometrium and decidua.

CASE RECORD

The patient, aged 23, married, nulliparous, was admitted to St. Luke's Hospital, Bradford, in January, 1952, with a complaint of lower abdominal pain and vaginal bleeding of a few hours' duration. The last menstrual period was about one month ago. Her previous health and family history revealed nothing of note.

She was thought to have an incomplete abortion and curettage was done. The scanty curettings obtained were not submitted for histological examination. Recovery was rapid and uneventful and she was discharged on the fourth post-operative day.

Six months later (8th June, 1952), she was readmitted with a history of 4 hours' lower abdominal pain and vaginal bleeding following 4 months' amenorrhoea. Her general condition was good, and there was no pyrexia. She was at first thought to have a threatened abortion but the persistence of bleeding and pain later suggested an incomplete abortion.

Dilatation and curettage on 10th June, 1952 provided copious curettings, thought to be obviously placental tissue; they were not submitted for histological examination. Thereafter the patient developed a remittent pyrexia, the evening temperature varying between 100° and 102° F. The scanty vaginal discharge yielded a growth of coliform organisms. Her urine was sterile on aerobic culture on routine media. X-ray examination of the chest at this time did not reveal any abnormality. The haemoglobin level was 85 per cent (13·6 g.).

The pyrexia continued despite the administration of penicillin, and, on the 30th June, 20 days after her second curettage, this was repeated. Histological examination of the curettings revealed tuberculous endometritis, together with products of conception (Figs. 1–4). From the appearances of the chorionic villi (Fig. 2), using the criteria of Anderson (1948), the period of gestation was estimated at about 10 weeks.

After this operation the pyrexia settled and the patient was discharged from hospital on 4th July, 1952.

Subsequent history

The patient attended the Out-Patient Department with reluctance in September, 1952, and reported that she was very well, that menstruation was normal, and that she did not wish any further treatment. She changed her address and difficulty was experienced in tracing her, but eventually, in January, 1953, she agreed to have her fourth curettage. At this time her menses were regular, occurring every 28 days but lasting for 7 days instead of 4. She had no complaints.

On admission there was thought to be slight diminution of breath sounds at the base of the right lung, but no other abnormalities were noted.

Pelvic examination under anaesthesia, on 12th January, 1953, revealed slight thickening of the tissues in the right fornix. Dilatation and curettage were performed, and the curettings again showed histological appearances typical of tuberculous endometritis.

X-ray examination of the chest on 15th January revealed the presence of a right pleural effusion, but there was no other evidence of pulmonary tuberculosis.

After curettage the patient was apyrexial except on three occasions when the evening temperature varied between 99° and 99·6° F.

On 29th January, 1953, she was transferred to a sanatorium where she was treated with streptomycin (46 g.) and para-amino-salicylic acid (P.A.S.). She was discharged on 24th April, 1953.

On 27th October, 1953, she again reported at St. Luke's Hospital with a history of amenorrhoea since 9th June, 1953. There were no clinical signs of pregnancy and the Hogben test was negative. She was feeling well and was putting on weight. The haemoglobin value was 80 per cent (12·8 g.), the erythrocyte sedimentation rate was 17 mm. after one hour and X-ray examination of the chest did not reveal any abnormality.

HISTOLOGY

Report on uterine curettings (3rd curettage, 30th June, 1952): "The curettings consist of fragments of both well preserved and necrotic

FIG. 1

Endometrial curettings (30th June, 1952). Endometrial tuberculosis (in square, right upper corner), chorionic and decidual tissue (left upper corner), and area of necrotic decidua in lower half of field. H. and E. ×35.

FIG. 2

Chorionic and decidual tissue. This depicts the same tissue as shown in Fig. 1 (left upper corner) but cut from the same block at a different level. H. and E. ×90.

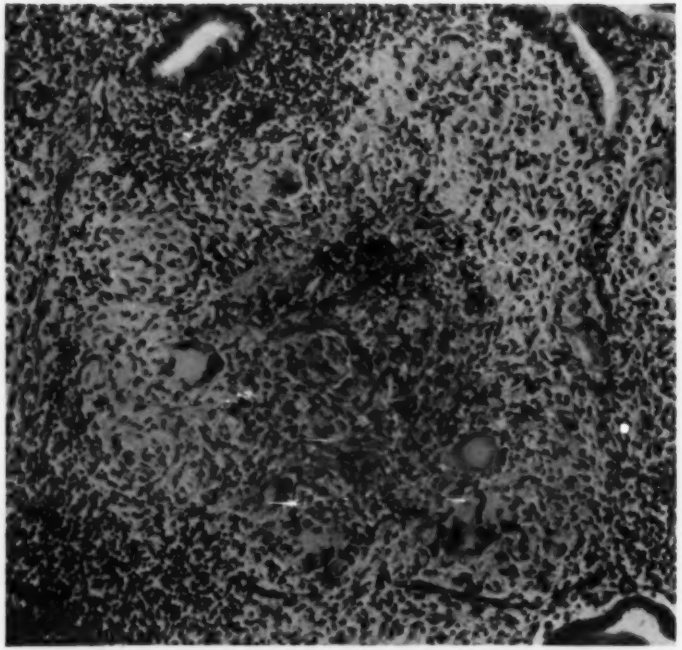

FIG. 3

Endometrial curettings (30th June, 1952). A typical tubercle follicle—a caseous focus surrounded by endothelioid-cells with giant-cells and lymphocytes at the periphery. H. and E. ×100.

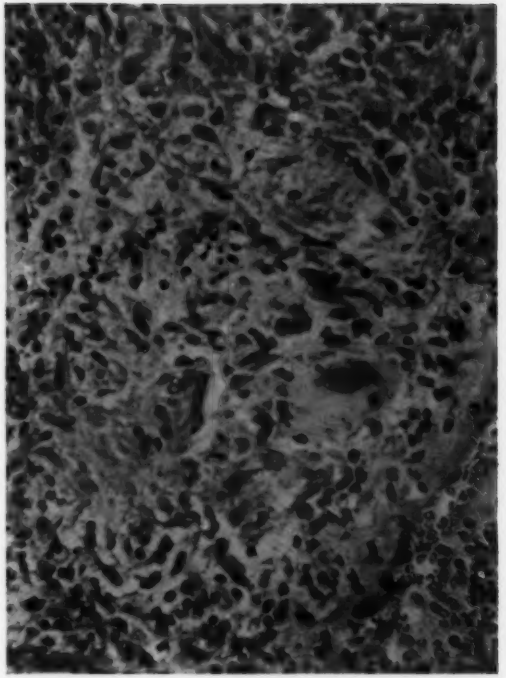

FIG. 4

The tubercle follicle depicted in Fig. 1. H. and E. ×300.

chorionic and decidual tissue. The bulk of the endometrium is non-secretory (oestrin phase): in the stroma there are numerous typical tubercle follicles. Acid-fast bacilli, morphologically resembling the tubercle bacillus (*Mycobacterium tuberculosis*), have been demonstrated in the tissues by the Ziehl-Neelsen method. The presence of doubly-refractive material has been excluded" (Figs. 1–4).

It is to be emphasized that, although histological appearances typical of caseating tuberculosis were present in the connective tissue of the decidua basalis and in the non-decidual endometrial stroma (Figs. 1, 3 and 4), the true decidual fragments showed no evidence of tubercle follicle formation although acid-fast bacilli were demonstrated in necrotic areas of decidua. The scanty chorionic tissues showed no inflammatory changes.

Report on uterine curettings (4th curettage, 12th January, 1953): "This is an endometrium in the non-secretory (oestrin) phase and shows appearances typical of an early caseating tuberculous endometritis. Acid-fast bacilli have again been demonstrated in the tissues."

Discussion

The finding together of tuberculous endometritis and products of conception could be interpreted in several different ways:

(1) By the establishment of pregnancy in a tuberculous uterus.

(2) By the spread of tuberculosis to the pregnant uterus from an infected Fallopian tube or other focus of infection in the body after the establishment of pregnancy.

(3) By a tuberculous infection of the uterus developing immediately after abortion or parturition with or without spread to retained products of conception.

In the present case, the second possibility is admitted in view of the slight adnexal swelling, possibly adnexal tuberculosis, detected in the right vaginal fornix in January, 1953. The third possibility, however, seems improbable in view of the extent of caseous change present in the tissues at the time of diagnosis.

The fact that the finding of endometrial tuberculosis, together with products of conception, has very rarely been reported (Mensing, 1936; Jedberg, 1950; Sutherland, 1952) suggests that the chance of pregnancy becoming established in a tuberculous endometrium must in fact be very slight.

Apparently normal secretory (progestational) changes have, however, been noted in tuberculous endometria (Schröder, 1921; Sutherland, 1943; Delarue and Bergerot-Blondel, 1949; Zander, 1949) and so there would seem to be no clear reason why the early stage of nidation of the fertilized ovum should not be possible. Should nidation occur, however, it must be assumed, in view of the lack of evidence to the contrary, that the presence of tuberculous endometritis interferes, somehow, with the subsequent development of the fertilized ovum and prevents continuation of the pregnancy.

In explanation of this, a hypothesis is put forward that a competition between hormonal (progesterone) and tuberculous stimulation for control of the stromal cells of the endometrium disturbs the balance existing between the infecting tubercle bacilli and the normally occurring defensive reaction of the tissues: consequently a necrosing spread occurs, rapidly and almost selectively, into this developing decidua and thus causes abortion early in pregnancy (within a few weeks). It has already been noted by Schmorl and Geipel (1904) and by Warthin (1907) that the reaction of decidual tissue to the presence of tubercle bacilli is characterized by necrosis and lacks the usual distinctive histological features (tubercle follicle formation).

The diagnosis of such early abortions may well be missed, the more so because many patients with tuberculous endometritis are accustomed to their menstrual irregularities (Sutherland, 1943; Eriksen, 1947; Stallworthy *et al.*, 1953).

Summary

Uterine curettings, obtained 3 weeks after an incomplete abortion, showed products of conception and histological evidence of tuberculous endometritis.

It is suggested that pregnancy may develop in a tuberculous endometrium more frequently than is realized, but that these cases escape detection because abortion occurs so early.

periphery. H. and E. ×100.

The hypothesis is put forward that this early abortion is due to rapid necrosis (caseation) occurring in the developing decidua.

One of us (R.A.McI.) would like to acknowledge his deep indebtedness to Professor A. C. Lendrum for helpful criticism in the preparation of this paper.

We also wish to express our sincere thanks to Mr. P. Harrison for the time and care spent in preparation of the photomicrographs, and also Mr. E. F. Hill for the preparation of the histological material.

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POST-PARTUM HAEMORRHAGE FROM UTERUS PSEUDO-DIDELPHYS

BY

D. B. WHITEHOUSE, M.A., M.D., M.R.C.O.G.

Senior Registrar

United Birmingham Hospitals

THE obstetrical complications that may result when pregnancy occurs in a double uterus are remarkable both for their number and variety. Several authors (Taylor, 1943; Hoffman, 1946; Fenton and Singh, 1952) have drawn attention to the increased risk of post-partum haemorrhage and retained placenta. This is generally attributed to the defective uterine musculature and also to the abnormal shape of the uterine cavity which interferes with normal separation.

An unusual cause of post-partum haemorrhage is incomplete separation of the decidual cast from the non-pregnant horn. That this may be a serious danger is illustrated by the following case.

CASE REPORT

A primigravida, aged 25 years, attended the antenatal clinic at St. Helier Hospital for booking on 2nd May, 1952 when 12-weeks pregnant. Her past health was normal and her general condition was quite satisfactory. The vulva was single but pelvic examination revealed a complete vaginal septum with a separate cervix at the vault of each vagina. A double uterus was present with a 12-weeks pregnancy in the right horn and the non-gravid left horn palpable separately below and to the left of it. No other obvious congenital defects were present. Routine investigations showed her haemoglobin to be 100 per cent and her blood group O Rhesus positive.

The pregnancy passed uneventfully and at 36 weeks the foetal head was fixed in the brim. The non-gravid horn of the uterus was palpable abdominally as a small globular swelling to the left of the pregnant horn. Pelvic examination indicated a normal pelvis and obstruction of labour by the non-gravid horn was considered most unlikely.

On 29th October, 1952, the patient was admitted with membranes prematurely ruptured at 38 weeks and the head engaged in the pelvis. Labour commenced soon afterwards and, following a first stage of 17 hours 30 minutes, the right cervix was fully dilated. As the head descended through the vagina, the vaginal septum split longitudinally close to the anterior wall. Its lower free edge, however, became tautly stretched over the vertex as the introitus was distended, thus delaying advance. Following division of this band and an episiotomy, spontaneous delivery occurred after a second stage of 1 hour and 40 minutes. The baby, a female weighing 6 pounds 8 ounces, was in good condition.

After a third stage of 10 minutes the placenta separated and was expelled complete, with a total loss of 4 ounces. The remnants of the vaginal septum were excised, the raw edges tidied with catgut sutures, and the episiotomy repaired in layers. Two hours after delivery the uterus was well contracted and there was no loss. The pulse was 62 and the blood pressure 110/85. Nine hours after delivery it was noticed that the mother's condition had deteriorated gravely. She was extremely pale, had air hunger and complained of pressure in the rectum. Her pulse was very weak and uncountable and her blood pressure was 80/50. Abdominal examination revealed a firmly contracted uterus but the level of the fundus was 3 inches above the umbilicus. The bed contained a large pool of blood and the vagina was found to be grossly distended by blood clot. Blood transfusion was immediately commenced and she was taken to the theatre.

Under general anaesthesia the vagina and uteri were explored. Thirty ounces of blood clot were removed from the distended vagina and amongst this was found an incomplete decidual cast from the left horn of the uterus. No source of bleeding was discovered in the vagina, but from the left cervix, which was 1-finger dilated, there was a steady trickle of blood. The left horn of the uterus was hypertrophied to the size of 12-weeks pregnancy and exploration of it produced several residual pieces of the decidual cast. The right, parous horn of the uterus was also explored but no retained products were obtained.

Following this operation and the transfusion of 2 pints of blood the patient's condition rapidly improved and gave rise to no further anxiety. Her lochial discharge was normal and she was discharged on the 14th day after an uncomplicated puerperium. At her postnatal visit, 6 weeks after delivery, both horns of the uterus were involuting normally, the right still being slightly larger than the left.

COMMENT

Although pregnancy in a double uterus is not common, a large number of cases have now been

reported in the literature to illustrate the abnormalities to which it predisposes. Among these may be mentioned abortion, twins, malpresentation, premature labour, inertia, obstructed labour due to the non-pregnant horn, ruptured uterus, and acute inversion of one horn.

The fate of the decidual cast varies. Not infrequently it is passed during pregnancy and a diagnosis of threatened or incomplete abortion may be made if a double uterus is unsuspected. In such cases an intact pregnancy may be inadvertently removed. The more usual course is for the cast to be discharged piecemeal in the lochia during the puerperium. When it separates complete, it is usually discharged between the fourth and tenth days of the puerperium.

It is possible that when early separation occurs and is incomplete, as in the case described, the risk of haemorrhage is greater because the uterine blood supply is still very generous.

Summary

A case is reported of severe post-partum haemorrhage caused by incomplete separation of the decidual cast from the non-pregnant horn of a uterus pseudo-didelphys 9 hours after delivery.

I should like to express my thanks to Miss Doreen Daley for permission to publish this case.

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POSTMATURITY AND HYPERTENSION

BY

J. D. MARTIN, M.D., M.R.C.O.G.

Late Assistant, Obstetric Unit, University College Hospital, London

THE difficulty of defining postmaturity has distracted attention from its dangers and prolongation of pregnancy past the expected date of delivery is now more generally realized to lead to complications. The most important of these is a rise in the stillbirth rate. This has been pointed out by many observers, Clayton (1941), Bickenbach (1947), Racker, Burgess and Manly (1953), and others. Karn and Penrose (1951), in a study of 13,730 single births at University College Obstetric Hospital from 1935-46, showed a significant increase in the combined stillbirth and neonatal rate associated with postmaturity. An extract of these findings has been made in Table I. The stillbirths and neonatal deaths have been considered together in their paper, and were referred to as non-survivors. This term will be used here. In the 2,000 cases forming the main substance of the present paper it has not been possible to show a significant difference in the mature and postmature non-survivor rates, owing to the small numbers of deaths.

The present paper concerns the investigation of non-survival of the foetus in postmaturity accompanied by hypertension in the mother.

DEFINITIONS

Patients were considered "hypertensive" if their diastolic blood pressure was 90 mm. Hg or over at any time during the antenatal period. No effort was made to separate the toxaemic patients from those with essential hypertension.

Postmaturity was defined as a period of gestation of 290 days or over following the first day of the last menstrual cycle. If there was any doubt about the date of the latter, the case was excluded.

Mature cases, with which it is possible to compare postmature cases, were defined as those delivered between 273 and 289 days after the first day of the last menstrual cycle.

MATERIAL

Five thousand four hundred and eighty-two records of deliveries at University College Obstetric Hospital between 1947 and 1951 were studied, and 1,000 postmature and 1,000 mature cases were collected. All multiple pregnancies were excluded.

RESULTS

Table II shows that the incidence of hypertension is not significantly increased in the postmature group. It must be remembered that a proportion of those patients induced with hypertension might have become postmature, and that other cases with hypertension have been induced before reaching maturity. Jameson and

TABLE I*

Gestation Time in Days	Males			Females		
	Total	Non-Survivors	Mortality per cent	Total	Non-Survivors	Mortality per cent
275–289	3,302	82	2·5	3,275	59	1·8
290–304	1,343	46	3·4	1,359	39	2·9
305 and over	351	17	4·8	312	10	3·2

* Reproduced by permission of Professor L. S. Penrose.

TABLE II

	Hypertensive (per cent)		Non-Hypertensive (per cent)
1,000 Mature (273–289 days)	21·9		78·1
	Over 90 mm. Hg Diastolic	16·7	
	Over 100 mm. Hg Diastolic	5·2	
1,000 Postmature (290 days+)	24·5		75·5
	Over 90 mm. Hg Diastolic	17·7	
	Over 100 mm. Hg Diastolic	6·8	

Handfield-Jones (1954) found 29 per cent of 566 patients had a diastolic blood pressure of 90 mm. Hg or more in pregnancy and 10 per cent one of 100 mm. Hg or more.

If the combined stillbirth and neonatal death rate is now studied in the two groups of 1,000 mature and 1,000 postmature cases, it is seen from Table II that maternal hypertension is an important factor in determining the survival of the foetus in the postmature case. Thus the non-survivor rates in both mature groups, hypertensive and non-hypertensive, and in the postmature group with no hypertension are all similar. But where there is hypertension and postmaturity the chances of survival of the foetus are reduced, the death rate in these cases being significantly greater than the mean death rate in the other three categories (u=1·76, P ·039*). When the group with hypertension and postmaturity is compared with only the postmature group without hypertension, the increase is not quite significant, but this is possibly due to the small number of cases considered (u=1·53, P ·063*).

A similar effect to that shown in Table III was obtained by considering a random group of non-survivors taken from the years 1935-46. The records of 118 such cases were examined and the results are set out in Table IV, showing a significantly larger proportion of deaths associated with maternal hypertension in the postmature than in the mature group (u=1·69, P ·046).

* One tailed test u is the "unit normal variable".

COMMENTS

There are other factors which have been considered partly responsible for this increase in non-survivor rate in postmaturity. Clayton (1953) has shown that in postmature cases there is an increased incidence of long labour and instrumental delivery; these two factors are probably related to one another, as long labours

TABLE III

	Totals	Non-Survivors	Death Rate per cent
Mature non-hypertensives	781	12	1·54
Postmature non-hypertensives	755	11	1·46
Mature hypertensives	219	3	1·37
Postmature hypertensives	245	8	3·27

TABLE IV

	Hypertensive Mothers	Non-Hypertensive Mothers	Total
Term. Non-survivors (273–289 days)	17 (31·1%)	36	53
Postmature. Non-survivors (290 days+)	32 (49·2%)	33	65

are more likely to be terminated by forceps delivery. Macdonald (1953) has contradicted the work of Josephs (1949) and has shown that the foetal head continued to grow progressively after the 36th week of pregnancy, and this might account for the increase in forceps delivery. If the 118 non-survivors from the years 1935-46 are considered and the forceps deliveries are removed from each group there are still 12 (33·3 per cent) hypertensives in the mature group and 22 (55 per cent) in the postmature group. Long labour can be treated in the same way and does not affect the conclusion that the hypertension is an important factor. Perhaps a more important reason for the increase in interference is the increased liability of the postmature group to foetal distress (McKiddie, 1949; Clayton, 1953; Dumoulin, 1953; Walker, 1954).

Discussion

The increase in non-survivors in postmaturity could be accounted for by the larger combined stillbirth and neonatal death rate in those patients with the combination of postmaturity and hypertension. This being so, these patients will require special supervision when threatening to become postmature.

At the present time in this country induction of labour, usually surgical, is most frequently employed in the treatment of postmaturity (Malpas, 1950; Racker *et al.*, 1953; Walker, 1954). If surgical induction of labour was without danger and could be carried out in every case with hypertension before the 290th day of pregnancy, it could be employed in these cases only, and the remainder left to go into spontaneous labour. But included in this series of patients with postmaturity and hypertension are a number who first developed their hypertension when already postmature, and therefore it might be too late for successful treatment. In addition, there are the risks of induction to be considered. Estimates of the foetal mortality attached to this procedure vary considerably. In America the Committee on Induction of Labour of the Central Association of Obstetricians and Gynaecologists (1939) reported this was 1·5 per cent for all inductions; for surgical induction alone, Maizels (1940) states it was 1·3 per cent, Dieckmann and McCready (1947) 0·7 per cent, and Hanley (1951) 0·5 per cent. Browne (1942) has warned us that we must be careful not to transfer mortality from one column to another by our antenatal care. Possibly careful supervision of the postmature patient with measures to avoid hypertension, close watch for signs of foetal distress during labour, and the earlier recourse to Caesarean section should distress develop, advocated by Clayton (1953), would yield results comparable with those obtained by induction of labour. Here it must be emphasized that in the past the more severe toxaemias were induced at or before term and only the milder case of hypertension, without albuminuria or severe oedema, ever reached postmaturity at this hospital.

Browne and Veall (1953) have shown that there is a decrease in placental blood flow in toxaemia of pregnancy, although in some of their cases the blood pressure was only slightly raised. Walker (1954) has also been able to show a reduction in the venous oxygen content and saturation of the cord blood in postmaturity. It seems reasonable to assume that the two factors operating together would form a more lethal combination and the present investigation supports this conclusion.

Obviously one reading of 90 mm. Hg diastolic blood pressure is a very rigid standard for hypertension, but it is undoubtedly outside the normal range as defined by Robinson and Brucer (1939), and should put the attendant on his guard, especially if the patient is approaching her 290th day of gestation. Unfortunately, experienced people do not always take the blood pressure in busy clinics and erroneous readings may be recorded. If a reading of 90 mm. Hg diastolic is recorded, this patient's blood pressure should be re-checked, and all patients who are postmature should have their blood pressure recorded frequently.

In view of the above findings it was decided as a trial at this hospital that no mother who had had a rise of diastolic blood pressure over 90 mm. Hg at any time in her pregnancy should be allowed to become postmature. In these cases the forewaters are ruptured at term.

Conclusion

If there is a reduction of the blood flow through the placenta in cases of postmaturity without hypertension, or some other factor operating to increase the combined neonatal and stillbirth rate, it is not important unless the postmaturity is reinforced by the presence of maternal hypertension. In this event, the foetus is more likely to die *in utero* or in the neonatal period.

Summary

(1) One thousand postmature and 1,000 mature cases were compared from the years 1947-1951, and the incidence of maternal hypertension was not significantly different in the two groups.

(2) Cases of postmaturity with maternal hypertension have a significantly greater non-survival rate than the mean death rate in postmature cases without maternal hypertension, and mature cases with or without hypertension.

(3) Considering a random group of 118 stillbirths and neonatal deaths from 1935-1946, death was significantly more frequently associated with maternal hypertension in those postmature.

(4) It is suggested that the larger death rate in the cases with postmaturity and hypertension could be responsible for the increased death rate observed in postmaturity.

(5) Particular attention should be directed to cases of postmaturity with maternal hypertension.

Acknowledgments

I am indebted to Professor W. C. W. Nixon and Mr. J. G. Dumoulin for their help and advice, and to Mr. N. W. Please, of the Department of Statistics, University College, London, for his suggestions and the statistical data. Table I is reproduced by permission of Professor L. S. Penrose.

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THE EFFECT OF DELAY IN THE FIRST STAGE OF LABOUR ON THE FORCEPS RATE AND ON THE STILLBIRTH AND NEONATAL MORTALITY RATES

An analysis of 4,401 consecutive primigravid labours at term, with 842 cases having a prolonged first stage

BY

E. I. OSTRY, *M.B.E.*, M.R.C.O.G., D.P.H.

Senior Registrar, Samaritan Hospital for Women, Marylebone Road, London, N.W.1

" If the disasters of midwifery could be traced back to their primary cause, it is probable that the majority of them would ultimately be ascribed to a failure of the dilating and expulsive forces of the uterus." (Bourne and Bell, 1933.)

WHAT constitutes delay in the first stage of labour? Definitions are as a rule based on the prolongation of the first stage beyond the average (Blair Bell, 1921), or beyond an arbitrarily chosen time such as 30 hours (Nathanson, 1935) or 48 hours (Eastman, 1947; Nixon, 1948).

Eastman (1947), in an effort to be more precise, states: "We define uterine inertia as follows: In the first stage, sluggishness of uterine contractions (after true labour has begun) of such a degree that—

(*a*) The cervix shows no change over an 8-hour period.

(*b*) The uterine wall is easily indentable at the acme of each pain."

He adds: "Uterine inertia and prolonged labour are not synonymous, because prolonged labour may be entirely normal and physiological, provided steady if slow progress is made. Uterine inertia, on the other hand, is complete prolonged absence of progress, in the presence of weak contractions."

While the above may be true, the clinical effects of delay on both the mother and foetus are hurtful, regardless of the cause.

Here an attempt is made to define delay, based on an analysis of 4,401 consecutive primigravid labours at term, in single pregnancies with the vertex presenting. Gross foetal abnormalities are excluded. Fig. 1 gives the numbers of these cases according to the length of the first stage.

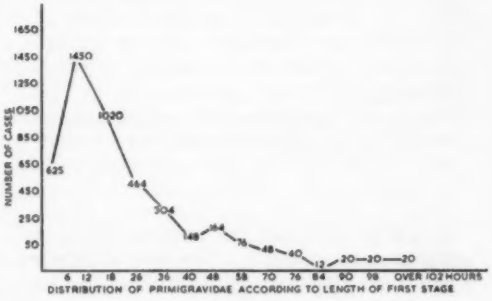

FIG. 1

It will be seen that this series is based on 842 cases of primigravid full-time labours with a first stage lasting more than 30 hours.

In Fig. 2 which relates the length of the first stage of labour to the forceps rate, we find a fairly steady rate of forceps delivery of between 5 and 6 per 100 cases until the 30th hour after the onset of labour.

After this time there is a rapid progressive rise, with the rate reaching 15 per hundred cases at the 36th hour, 20 per 100 cases at the 48th hour and 30 per 100 cases at the 72nd hour.

In Fig. 3 the neonatal death and stillbirth rates are related to the length of the first stage. Premature labours and death *in utero* before the onset of labour are excluded.

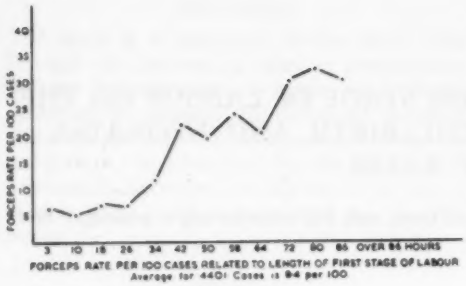
FORCEPS RATE PER 100 CASES
40
35
30
25
20
15
10
5
3 10 18 26 34 42 50 58 64 72 80 86 OVER 86 HOURS
FORCEPS RATE PER 100 CASES RELATED TO LENGTH OF FIRST STAGE OF LABOUR
Average for 4401 Cases is 8·4 per 100

FIG. 2

STILLBIRTH & NEONATAL DEATH RATE PER 100 CASES
18
16
14
12
10
9
8
6
4
2
3 10 18 26 34 42 50 58 64 72 80 86 OVER 86 HOURS
STILLBIRTH & NEONATAL DEATH RATE PER 100 CASES RELATED TO LENGTH OF FIRST STAGE (Average 1·9 per 100 Cases)

FIG. 3

It will be seen that the neonatal death and stillbirth rates remain at a low level of between 1 and 2 per 100 deliveries until about the 30th hour. Thereafter, there is a steady progressive rise reaching 4 per 100 at the 36th hour, 7 per 100 at the 48th hour, 13·5 per 100 at the 72nd hour and 14 per 100 after 76 hours. The average over the whole series is 1·9 per 100 cases. These figures emphasize those of Nixon (1952), except that they show the increase of foetal loss starting some 6 hours earlier than his.

From the above it would seem that the advent of the 30th hour in the first stage of labour witnesses a dramatic change in the prognosis both to mother and child, a prognosis that deteriorates with each passing hour.

The treatment of delay in the first stage of labour is on the whole disappointing. From the above figures it seems apparent that, if labour is not progressing rapidly after the 24th hour in spite of adequate care, a more active type of treatment should be carefully considered.

Further studies may well point to the increasing foetal hazards with a prolonged first stage as being peculiar to a specific factor, such as a hypertonically acting uterus, and not associated with all types of delay.

SUMMARY

(1) A first stage of labour up to the 30th hour carries no appreciable increased risk to the foetus and no raised forceps rate.

(2) Delay of the first stage beyond 30 hours increases the forceps rate. This rate increases with each passing hour, with all attendant hazards to mother and foetus.

(3) The stillbirth and neonatal death rates increase after prolongation of the first stage beyond 30 hours and the numbers of these disasters increase with each passing hour.

(4) If stillbirth and neonatal death rates from this cause are to be reduced, then every case that is still in the first stage of labour after 24 hours must be considered delayed. At this time it should be carefully reassessed and, if cervical dilatation does not progress rapidly and steadily, more active steps should be undertaken to complete delivery by the 30th hour. The type of active interference will vary with the individual case.

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Obituary

DONALD McINTYRE

M.B.E., M.D., F.R.C.O.G., F.R.C.S.E., F.R.F.P.S., F.R.S.E.

DR. DONALD MCINTYRE, Senior Gynaecologist at the Royal Samaritan Hospital for Women, Glasgow, died in a Glasgow Nursing Home on 20th October, 1954. He was 63 years of age.

Donald McIntyre was born on 29th July, 1891, in Greenock, and was a student at Glasgow University, where he graduated M.B., Ch.B., with commendation, in 1914. He entered the R.A.M.C. and served for four years in the first world war in the Dardanelles campaign and in East Africa, being appointed M.B.E. in 1918 and mentioned in dispatches. On demobilization he was granted the rank of honorary major. Returning to civilian life, McIntyre devoted himself to the study of obstetrics and gynaecology, taking the diploma of L.M. at Dublin in 1919 and the F.R.C.S.Ed. in the following year. He joined the staff of the Royal Samaritan Hospital for Women, Glasgow, in 1920 as pathologist, a post which he held for seven years. In 1921 he became a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow, and in 1926 he proceeded to the M.D., with honours, being awarded the Bellahouston Gold Medal for his thesis. In the following year he gained the Struthers Gold Medal and Prize from Glasgow University and was elected a Fellow of the Royal Society of Edinburgh. In 1923 he was appointed assistant surgeon to the Royal Samaritan Hospital for Women, and four years later he became surgeon in charge of wards. McIntyre had been senior consulting gynaecologist to the Royal Samaritan Hospital for Women since 1936, and a member of the board of management of the Glasgow Maternity and Women's Hospitals Group since the inception of the National Health Service. Other appointments he held were Royal Samaritan Lecturer in Gynaecology, Glasgow University; consulting obstetric surgeon, Barshaw Maternity Hospital, Paisley, and to the County of Renfrew; examiner to Glasgow University, the Royal Faculty of Physicians and Surgeons of Glasgow, the Central Midwives Board for Scotland, Edinburgh University, and the Royal College of Surgeons of Edinburgh. He had previously held appointments as visiting surgeon, Royal Maternity and Women's Hospital, Glasgow, and first assistant to the Regius Professor of Midwifery, Glasgow University. In 1931 McIntyre was elected a Foundation Member of the newly established College of Obstetricians and Gynaecologists, becoming a Fellow of the College in the following year. At the Annual Meeting of the British Medical Association held at Cambridge in 1948 he served as a vice-president of the Section of Obstetrics and Gynaecology. He wrote a number of monographs and was part author of *Operative Obstetrics* (1937), and *Combined Textbook of Obstetrics and Gynaecology* (1950).

He always maintained close contact with the Embryological Section of the Anatomy Department of the University of Glasgow and indeed was well known and recognized as an authority on many aspects of the early development of the human embryo. He was an enthusiastic and well-informed authority on embryology. Two of the most beautiful specimens in the Glasgow collection—McIntyre I and McIntyre II—were given to the Department back in the 20s in the time of Prof. T. H. Bryce. The McIntyre I, an embryo of about 1·4 mm. provided the material for a Monograph by Bryce—"Observations on the Early Development of a Human Embryo", published in the Transactions of the Royal Society of Edinburgh in 1924. This embryo at that time ranked as one of the youngest human specimens. From the same specimen he recorded

his observations, "The Development of the Vascular System in the Human Embryo Prior to the Establishment of the Heart", also published in the Transactions of the Royal Society of Edinburgh in 1926.

He served on numerous governing bodies, where his wise counsel was much appreciated. As a teacher, operator and research worker he was first-class. A warm and generous host, he loved entertaining, revealing a charming and stimulating personality. In his younger days he enjoyed golf, but during his latter years he turned for recreation to yachting and lobster-fishing. One of his great joys was a trip to Murrayfield to watch an international Rugby match, which he rarely missed. In his illness his fortitude was beyond praise.

He had an extensive practice in Glasgow and the west of Scotland. He married in 1922 Miss Jean Menzies who survives him with their son; to them we extend our deep sympathy.

ALBERT SHARMAN

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of Council was held in the College House on Saturday, 29th January, 1955, with the President, Sir Arthur Gemmell, in the Chair.

William Meredith Fletcher Shaw Memorial Lecture:

Professor B. P. Watson, M.D., F.R.C.O.G., New York, was appointed lecturer for 1955.

The following were elected to the **Membership of the College:**

Robert Henry Obuabasa Bannerman.
David Barron.
Henry Robert Clifford Benny.
David Byron Brown.
Thomas Ian Cope.
Alan Cameron Coulthard.
Keith Douglas Drayton.
William Allan Webb Dutton.
Brian Alan Gavourin.
Herbert Samuel Gavourin.
Tara Sankar Ghosh.
Antony Plumer Brunyee Harston.
Beryl Overton Howie.
Beryl Mary Joles.
Mukulika Konar.
Wendy Ellen Lewington.
John Dilwyn Llywelyn-Jones.
Philippa Mary Ludlam.
Colin Ferguson Macdonald.
John Gordon Mathie.
Appuahandy Ariyaman Mahanama Mendis.
David Methuen.
Catherine Hutcheon Mitchell.
Nanda Gopal Mukherjee.
Rathindra Nath Nag.
Chiew Seng Oon.
Shephalika Prodhan.
Richard Tankard Sears.
Harendra Bahadur Sinha.
David Henry Kenneth Soltau.
Oswald Selwyn Treisman.
Yin-Kai Tsao.
John Kitching Tully.
Jacobus Adolf Mangold Van Belkum.

The following have been awarded the **Diploma in Obstetrics:**

Louis C. Steindel.
Derek Charles Wilkins.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

October 1954

The Meeting of the North of England Obstetrical and Gynaecological Society held in Manchester on Friday, 15th October, 1954, with the President, Mr. K. V. Bailey in the Chair, was devoted to two debates.

Mr. G. W. Theobald (Bradford) proposed:

THAT EXTERNAL VERSION IS A USEFUL AND DESIRABLE PROCEDURE

Mr. Theobald pointed out that, if all patients were delivered by experienced attendants in good surroundings, the foetal mortality in breech might be so low that antenatal external version might not be justified. Unfortunately this ideal had not yet been reached. Successful external version, therefore, allowed the patient to be delivered at home, whereas failure to turn should be an indication for delivery in hospital. Version itself was not entirely free from risk, but particularly in cases of doubtful disproportion it was justifiable even under anaesthesia, because a head presentation in these cases enabled a trial labour to be carried out with greater ease and judgment.

Mr. C. R. Macdonald (Grimsby), opposing the motion, said that a high rate of spontaneous version rendered external version largely superfluous. Breech delivery was not very hazardous if all precautions were taken. The foetal loss was most commonly due to causes other than the presentation itself, such as foetal abnormality, or prematurity. Further, the patient who was subjected to attempts at external version, perhaps repeatedly, was at a psychological disadvantage as she was liable to think that something was seriously wrong with her pregnancy.

Mr. H. R. Arthur (Newcastle) deplored the use of one dangerous procedure to prevent another dangerous procedure. Version might easily be practised too early and too often, and anaesthetics provided a temptation to use more, not less, force.

Miss Crystal Bates (Nottingham) enumerated the hazards of external version. She said it was more important to teach how to deliver breeches than how to perform external version.

Professor T. N. A. Jeffcoate (Liverpool) followed this up by pointing out that in teaching hospitals successful external version might limit the opportunities to teach and learn the art of breech delivery.

Professor W. I. C. Morris (Manchester) concluded for the proposition. The essential point was that one did not contemplate a breech in labour with the same equanimity as a head presentation. Antenatal version was therefore useful and desirable, and if anaesthesia were employed it allowed a full clinical assessment of the pelvis at the same time.

Dr. R. Newton (Manchester) proposed:

THAT PELVIC EXENTERATION IS NEVER JUSTIFIABLE

Dr. Newton outlined the forms of treatment available for radioresistant and recurrent cases of pelvic carcinoma. It had been shown that it was possible for a woman to survive pelvic exenteration—but at what cost to her! The operative mortality was high, but even if the technical difficulties could be overcome and the operation were carried out only by those with the necessary skill and experience the end results did not justify such physical and mental trauma. What, he asked rhetorically, was the ultimate aim of ultraradical surgery?

Dr. R. B. Burslem (Manchester), in opposition, explained that the operation was based on the fact that in over 30 per cent of women who died from carcinoma of the cervix there were no extra-pelvic metastases. He admitted that the operation was still in the experimental stage but claimed that any salvage in these desperate cases was a victory. He detailed 5 cases in the care of which he had been associated, pointing out the hazards and remarking that anterior partial exenteration seemed to entail a higher mortality than the total operation, probably because of the greater difficulty in maintaining electrolyte balance post-operatively. He was supported by

Mr. P. C. Steptoe (Oldham) who gave details of 9 personal cases. If searching investigations were first made, the operation was undoubtedly sometimes justified.

Mr. H. S. Waters (Blackburn) had had no direct experience of the operation but he thought that published results justified it. The patient should be given the choice. Even if the mortality was not inconsiderable it might be a happy release for some patients.

Mr. D. W. Currie (Leeds) remarked that the difficulty lay in the choice of case, for how could one be sure there was no extra-pelvic spread. Surgical technique must never outstrip commonsense. Finally

Professor C. S. Russell (Sheffield) said that the subject must be discussed on a personal, not a statistical basis.

BOOK REVIEWS

"Office Gynecology." By J. P. GREENHILL, B.S., M.D., F.A.C.S., F.I.C.S. Sixth edition. Pp. 517 with 157 figs. Year Book Publishers, Chicago, U.S.A., 1954. Price 60*s*.

THE appearance of a sixth edition of this book 15 years after its first publication is ample evidence of its proved popularity on the American continent. The latest edition, partly re-written and completely revised, is like its predecessors a companion volume to *Surgical Gynecology* which comes from the facile and prolific pen of the same author.

Any book which aims at including "everything which a practising physician or a gynecologist should know concerning the practice of gynecology in an office or out-patient surgery room" is likely to be scanned less for omissions than for transgressing its scope. Despite Dr. Greenhill's obvious desire to save patients the expense of unnecessary hospitalization, he has not stretched the sphere of consulting room or out-patient gynecology beyond the bounds of safe practice. The only criticism that might be voiced in this respect is that it may be wiser when dealing with cervical polypi, especially in women past the menopause, also to curette the uterus.

The practitioner in this country will probably find those chapters most useful to him which discuss subjects dealt with less fully in similar British textbooks. Let him not be deterred by the opening comprehensive list of "office equipment necessary for gynecologic practice", starting with "Examination table" and ending, five pages later, with "Rug outside the door for wiping shoes on rainy or muddy days". Let him persevere to discover a wealth of practical instruction and to find a clear account of gynaecological endocrinology which successfully avoids both over-scepticism and over-optimism. And if he persists to the end he will be rewarded by an excellent concluding chapter on premarital examination and advice, a subject on which undergraduate and post-graduate teaching in this country is usually deficient.

"Diagnostic Cytologique du Cancer Génital chez la Femme." (Cytological Diagnosis of Genital Cancer in Women.) By RAYMOND BOURG, CLAUDE GOMPEL and JEAN-PAUL PUNDEL. With a Preface by Charles Oberling. Pp. 183, plus atlas. Masson & Co., Paris, 1954. Price £5 5*s*. 6*d*.

THIS is the first considerable book in the French language on the cytological diagnosis of genital cancer. Professor Bourg of the University of Brussels has made a prolonged study of the subject of vaginal cytology and this volume represents many laborious years of work.

The text is very clearly written and includes a detailed description of the techniques he employs in cytological diagnosis including staining methods. The cytological characteristics of cancer cells are most carefully described and also the appearances in associated conditions, as for example the effects of irradiation.

He reaches the wise conclusion that the results of cytology must be considered together with the clinical findings and that the ultimate diagnosis of malignancy must rest on biopsy.

The book is beautifully illustrated with an atlas comprising 83 plates and a chart showing the types of cells encountered in vaginal smears from normal and abnormal cases.

This book, which is so simply written and so well illustrated, can be warmly recommended not only to those with a special interest in vaginal cytology but to all practising gynaecologists.

Josephine Barnes

"Man's Capacity to Reproduce. The Demography of a Unique Population." By JOSEPH W. EATON and ALBERT J. MAYER. Pp. 59. The Free Press, Glencoe, Illinois, 1954. Price $2.

THE study of human fecundity, that is the maximum capacity to reproduce restrained only by biological factors, is severely restricted by the paucity of relevant data. For those countries where census and vital statistics are detailed and accurate, the predominant factors influencing reproduction are social and economic; whilst in those countries in which the effect of these factors is at a minimum, the available statistics are in general fragmentary. The ethnic Hutterites of North America are a rare exception to these general rules.

As a by-product of research into "Cultural and Psychiatric factors in the Social Life of the Hutterites", extensive demographic data of the group was collected in 1950 and an analysis of these data is now available. From the acknowledgments and other references in the book, it is made clear that the authors wisely sought the cooperation and advice of a wide range of recognized experts, and they have thereby avoided the many pitfalls with which so complex a study is beset. It is also important to mention that the close cooperation of the Hutterites themselves was obtained, without which both detailed and accurate data would not have been forthcoming.

The rarity of such complete data on so interesting a group gives to the book a value out of proportion to its size—it is of only 59 pages.

Between 1870 and 1880, almost all the surviving Hutterites fled to North America from religious persecution which had almost exterminated the sect. At the 1880 census of the U.S.A., 443 Hutterites were enumerated in closely knit communities. In 1950 their descendants numbered 8,542, representing a rate of increase unprecedented in statistical history and probably in all time. The rate of increase for the most recent decennium,

1941–50, was over 4 per cent, and there are but small indications of any tendency for fertility rates to decline. The married women most recently to complete their childbearing life—those aged 45–49 in 1950—had borne 10·9 children each on average, including some 2 per cent who were childless. Notwithstanding their high fertility, the mortality of the group is low; today it is similar to that of the white population of the U.S.A.

The book includes numerical data (there are 20 small tables) but, to avoid disappointment, the reader must be warned not to expect too much. The small size of the group prevents analysis of the data in fine sub-divisions, so that occupational differentials and causes of death, for instance, are hardly mentioned. The authors have appreciated on the one hand the interest in these subjects, and on the other the unreliability of their data in fine sub-divisions, and, whilst mentioning the subjects, have not attempted to draw unwarranted conclusions.

N. H. Carrier

"Clinical Measurement of Uterine Forces in Pregnancy and Labour." By S. R. M. REYNOLDS (Baltimore), J. S. HARRIS (Denver), and I. H. KAISER (Minneapolis). Pp. xiv+328, 99 figures. Charles C. Thomas, Springfield, Illinois, U.S.A. and Blackwell Scientific Publications, Oxford, 1954. Price 69*s*.

THE work of Reynolds and his several collaborators—including Harris and Kaiser—on uterine motility is already well known. The basis of Reynolds's studies is that the exact nature of uterine activity can only be revealed by some system of multi-channel recording. In numerous communications he and his co-workers have given their experiences using a "multi-channel strain-gage tokodynamometer" and described what they consider to be the detailed pattern of uterine activity in various circumstances. Now, in a single convenient volume, the substance of these several papers is reviewed and, with some other material, is presented as an orderly account of the authors' methods and findings, together with a survey of their opinions on the true pattern of uterine contractility in normal and abnormal pregnancy and labour.

The book is arranged in four parts. The first part comprises an adequate historical review of all the methods of recording uterine activity which have been described to date, followed by a chapter setting forth the authors' views on the physiological basis of tocography.

The second part deals fully with selected methods of tocography, on the results of which the authors base their deductions. These include Alvarez and Caldeyro's transabdominal method of measuring intra-amniotic pressure and a trans-cervical recording based on Williams's and Stallworthy's method, while there is a brief account of Karlson's work.

The external tocograph described is the complicated and costly "multi-channel strain-gage tokodynamometer", in which movements of three plungers applied to the abdominal wall are transmitted to the strain gauges and by suitable electronic magnification graphically recorded. A subsequent chapter deals with the activity of the uterus in pregnancy and labour as demonstrated by internal tocography. There can be no denying that the changes in intra-uterine pressure so demonstrated reflect accurately the behaviour of the uterus as a whole. The changing pattern of contractility with growing prominence of the Braxton-Hicks or major (as opposed to minor) contractions, culminating in those of labour, is interpreted by the authors as an increasing degree of coordination of the myometrium resulting from synchronism of its several parts.

The third part of the book sets forth the authors' opinions on the detailed pattern of uterine contractility during normal and abnormal pregnancy and labour, based on their experiences of multi-channel external tocography. Reynolds and his colleagues claim that normal uterine activity is always characterized by "fundal dominance" and "a gradient of activity" from fundus to cervix. This may well be but there may remain in the reader's mind some doubt as to whether external tocography is an entirely satisfactory means of demonstrating it. It is not altogether certain what external tocography measures. Reynolds implies that during contraction of the uterus there is a diminution in its radius of curvature but, as Halliday and Heyns have pointed out in a recent paper, if there is, in fact, dominance of the upper segment, application of Laplace's formula shows that its radius of curvature must increase.

One wonders if there is not a real danger of reading too much into the results of external tocography—especially a comparative multi-channel method. It is perhaps a reflection of this danger that, while Murphy made much of the ability to measure uterine tone with an external tocograph, Reynolds and his co-authors make no claim to be able to do so; neither do they think it possible to forecast the course of labour from tocographic records of pregnancy. It must be remembered that whatever is measured is recorded through the abdominal parieties, the varying thickness of which must influence the recording and, one would have thought, any gradient of activity. Again it is to be noted that the usual sites for the three receptors in the upper, middle and lower segments of the abdomen do not necessarily correspond with the upper, middle and lower uterine segments. The reader may question whether the usual lack of activity in the lowest receptor is to be attributed to an inactive lower uterine segment or to the inter-position of soft parts between the uterus and plunger.

The second concept in the authors' thesis regarding the character of uterine motility in normal labour is that there should be close synchronization and coordination of activity in the several parts of the uterus. Certainly this is in accord with the present-day view that inefficiency of the expulsive forces is mostly the result of incoordinate uterine action and multi-channel tocography has provided a certain amount of evidence to support it. Whatever the inherent defects of external tocography, it must be admitted that the authors bring a great deal of evidence to support their thesis and they are to be congratulated on the thoroughness with which they have analyzed and presented the results of a vast experience of tocography.

A concluding section in which the authors deal with the effects of emotional influences and certain drugs on

uterine activity is especially good. They do a particular service in drawing attention to the importance of psychomatic factors and the need for adequate controls in clinical studies, while the observations on adrenaline shed light on the seemingly contradictory opinions previously expressed regarding this drug.

Mostyn M. Embrey

"The Mechanism of Labour." By ERIK RYDBERG, M.D., Professor of Obstetrics and Gynaecology, University of Copenhagen, Denmark. Pp. xii+180 with 38 figures. Charles C. Thomas, Illinois, U.S.A., and Blackwell Scientific Publications, Ltd., Oxford, 1954.

IN 1935 this Journal published Professor Rydberg's account of the investigations which led him to believe that the usual mechanism of labour in vertex presentations can be ascribed to the shape properties of the foetal head. In this monograph, published as one of the American Lectures in Gynecology and Obstetrics Series, his creed is enlarged upon by argument and experiment, illustrated by motion-picture and radiograph and supported by detailed geometrical exposition.

The traditional description of the mechanism of labour is examined and largely rejected. Flexion is held to be an inconstant and varying feature of engagement and descent; in the later stages of descent the cervical and upper dorsal spine are shown by radiographs to be straight or lordotic in almost all cases. The theories of Sellheim, Young and others, commonly accepted in the interpretation of the phenomenon of internal rotation, are said to be of limited validity and then only in exceptional cases. External rotation of the head is seen on motion-picture study to be often incomplete and sometimes absent, while the shoulders are expelled in the oblique diameter in about 30 per cent of cases and in the transverse diameter not exceptionally.

The author proceeds to a comprehensive analysis of the shape properties of the foetal head, and gives his reasons for holding that the characteristic bean-shaped asymmetry of the foetal head is normally the chief factor in determining its movements during labour. He assumes from his experimental models that the birth canal has the same "deformability" as a curved tube of a homogeneous elastic material.

The basic mechanisms of labour are no esoteric study but are phenomena which the thinking obstetrician must seek to understand. Professor Rydberg, who has not neglected the historical background of his subject, has in his approach combined theoretical argument and practical observation in lucid fashion.

"Childbirth: Theory and Practical Training." By MARJORIE F. CHAPPELL, D.N.(Lond.), S.R.N., C.S.P., S.C.M., H.V.Cert. Pp. viii+128, with 35 figures. E. & S. Livingstone, Ltd., Edinburgh, 1954. Price 7*s.* 6*d.*

THERE is now a fair amount of literature on the themes generally described by such titles as "Natural Childbirth" or "Training for Childbirth", but there is room for more. It is always helpful, for example, to have an analysis of the results of some scheme of training, or a comparison of different schemes; or to hear of improvements or changes of methods—which are now generally based on the same original patterns; or to be given a restatement or reassessment of the whole subject from a new angle. Even a clear statement of one scheme is useful, especially if there is some probing into the reasons for results and for choice of method.

Mrs. Chappell's book does not quite do any of these things. She does explain in detail, and with many personal touches, how she applies well-known methods to her own classes, which she has been conducting for some years and which one can imagine are most successful. There is, however, little critical assessment of methods previously described, which have been accepted wholesale, including even such exercises as "bicycling in the air" for postnatal rehabilitation—a practice now generally condemned. There are some surprising inaccuracies, such as the statement that it is expiration which releases the gas in gas and air machines. The language is exceptionally awkward. The reviewer feels that in this book an opportunity has, on the whole, been lost.

REVIEW OF CURRENT LITERATURE

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PHYSIOLOGY

1. Reflections on the Physiology of Menstruation.
By C. E. McLennan. *J. Amer. med. Ass.*, **156**, 578-580. Oct. 9, 1954. 8 refs.

A precise definition of menstruation is difficult because there are at least two different points of view to be considered. Many authorities believe that any periodic bleeding, with or without ovulatory cycles, in the absence of pregnancy constitutes "normal" menstruation. Others, including the author, regard true menstruation as regular recurring bleeding of limited duration originating from progestational (secretory) endometrium. The clinician is only as a rule concerned with periods of bleeding that are profuse, prolonged, scanty, irregular, or persistent. Many of these represent the breakdown of an endometrium unaffected by progesterone, and are therefore not true menstruation. Although some episodes of anovular bleeding can mimic menstruation almost completely these are seldom disturbing to the patient and are therefore seldom seen in practice. There are differences between ovulatory and anovulatory bleeding that can be of genuine aid in solving clinical problems.

Most normal menstrual cycles are within the range of 20 to 35 days, and the flow rarely persists for more than 7 days. The shedding of secretory endometrium is usually preceded by a characteristic train of symptoms and although there is wide individual variation these characteristics are reasonably constant for any one person and a little time devoted to the details of these simple matters may be rewarding.

Knowledge of the basic physiology of menstruation is incomplete, especially with regard to the humoral-neural-vascular mechanism, the histological changes, and the manner in which cholinergic and adrenergic drugs affect the endometrium and ovaries. The author believes, however, that a more general acceptance of true menstruation as a limited physiological phenomenon (associated only with ovulation) would improve judgment about uterine bleeding as it is seen in pathological states.

D. W. James

PREGNANCY

2. The Psychology of Pregnancy and Psychological Causes of Postmaturity. (Zur Psychologie der Gestation und zur Frage der Schwangershaftsübertragung aus psychologischer Ursache.)
By C. Müller. *Gynaecologia, Basel*, **138**, 447-465. Oct. 1954. 29 refs.

The author, discussing the psychological changes which occur in normal pregnancy and labour, concludes that the normal changes are important for the preservation and continuation of the human race.

Abnormal psychological reactions are common. Among these fear is by far the most important and the

fear of death is outstanding. Every pregnancy brings about psychological changes and in the unstable woman these may be serious.

Three cases are reported where postmature pregnancy appeared to result from psychological conflict. The author believes that "retention" of the infant from fear or from other deeper motives is an important factor in postmaturity.

Josephine Barnes

3. **Prolonged Pregnancy.**

By L. G. HIGGINS. *Lancet*, **2**, 1154–1156. Dec. 4, 1954. 9 refs.

The author records a well authenticated case of pregnancy lasting 1 year and 24 days and ending in delivery of an anencephalic monster. Delivery was effected by Caesarean section for delay in the 2nd stage of labour in spite of good contractions. The author quotes other cases of prolonged pregnancy which have been reported from time to time.

H. H. Fouracre Barns

4. **Grand Multiparas.**

By E. MILLER. *Obstet. and Gynec.*, **4**, 418–425. Oct. 1954. 9 tables. 9 refs.

This study of 563 grand multiparas from the Catholic Maternity Institute, Santa Fé, New Mexico, considers women who have delivered 6 or more viable infants. Many were delivered at home. From a total of 2,303 deliveries, the distribution by parity is given as follows:

Parity	*Percentage*
6	6·3
7	5·3
8	4·0
9	3·4
10	2·2
11	1·4
More than 11	1·8

Of the 563 grand multiparas 85 per cent had normal labours. The incidence of breech presentation was 3·5 per cent, and of face, brow and transverse 1·9 per cent. Abruptio placentae occurred in 2·1 per cent, placenta praevia in 1 per cent and post-partum haemorrhage (500 ml. or more) in 8·3 per cent. The incidence of manual removal was 1·6 per cent. There was 1 maternal death in the whole series, no case of ruptured uterus, and the stillbirth rate was 1·9 per cent. Caesarean section was done 12 times (2·1 per cent), 7 for abruptio placentae. The incidence of prematurity was 8·8 per cent, and it increased with the age of the mother. Hypertension, renal disease and associated conditions occurred far less frequently than other investigators have found.

J. G. Dumoulin

5. **Gastric Acid and Plasma-Histaminase During Pregnancy.**

By D. H. CLARK and H. I. TANKEL. *Lancet*, **2**, 886–887. Oct. 30, 1954. 3 figs. 1 table. 13 refs.

The authors point out that pregnancy may exercise a favourable effect on the course of peptic ulcer and hence considered that the improvement might be due to the action of histaminase, an enzyme which inhibits histamine and thus reduces the secretion of acid. The authors therefore investigated whether acid secretion (spontaneous and histamine induced) is regularly reduced during pregnancy and whether any such change is related to the plasma-histaminase level. Nine patients were fully investigated every 4 weeks during pregnancy from about the fourteenth week onwards and on several occasions after delivery. Two of the patients had a peptic ulcer history and the other 7 had no such history. Only in 1 patient was there a significant fall in the acid content of the gastric juice during pregnancy, in 5 there was no significant difference and in 3 there was a significant rise. The plasma-histaminase level was consistently raised during pregnancy in all 9 patients. The authors conclude that there is no justification for the belief that the acid secretion of the stomach regularly diminishes during pregnancy and that there is no correlation between the plasma-histaminase level and the amount of either spontaneous or histamine-induced gastric secretion.

H. H. Fouracre Barns

6. **Preliminary Report on an Investigation of Foetal Electrocardiography and Foetal Stethography.**

By J. DAVIS and S. DEVENISH MEARES. *Med. J. Aust.*, **2**, 501–504. Sept. 25, 1954. 5 figs. 11 refs.

The development of foetal electrocardiography and its application appear likely to be of greater importance to the obstetrician than the paediatrician.

From 32 attempts in the foetal age group of 17 weeks to term satisfactory electrocardiograms were obtained in over nine-tenths of the cases investigated.

Foetal electrocardiography may also determine whether the foetus presents by the breech or vertex, and whether the pregnancy is multiple.

The four tracings reproduced have been reduced to approximately one-third the size of the recordings for publication.

In the investigation at Sydney Hospital, the authors use a six channel electroencephalograph in conjunction with electrodes for electrocardiographs.

Five abdominal electrodes are used and one vaginal one.

The abdominal ones are of two types, one of flattened solder pellets, and the other of small cup-like suction cups or "limpet electrodes". Both are applied with electrode paste. The vaginal one is a solid metal sphere with a projection on one side connected to the end of a piece of rubber tubing with a piece of wire passing from the sphere along the bore of the rubber tube.

The apparatus for foetal stethography is a specially adapted crystal microphone used in conjunction with the electroencephalograph. Both foetal stethograms and electrocardiographs can be recorded simultaneously.

S. Devenish Meares

7. **Gunshot Wounds of the Pregnant Uterus.**

By A. J. KOBAK and C. H. HURWITZ. *Obstet. and Gynec.*, **4**, 383–391. Oct. 1954. 4 tables. 28 refs.

The world's literature on gunshot wounds of the pregnant uterus is reviewed by the authors who present 2

additional cases, a total of 33 cases. There were 3 maternal deaths, none occurring after 1912. Bowel perforations were found in 8 cases and bladder wounds in 2. Conservative management without laparotomy was carried out in many of the earlier cases. Of 7 patients so treated none died (somewhat fortunately!). Laparotomy should always be done in any penetrating gunshot wound of the abdomen. The uterine injuries were repaired in 8 cases, the foetus being delivered vaginally. In 15 women Caesarean section was performed with 2 maternal deaths: in 3 women hysterectomy was done. Of the 22 foetuses 7 months old or over, 10 survived. In discussing the treatment of injuries of this nature, the authors consider that the factors which must be considered are the condition of the foetus and mother and the extent of injury to the uterus.

J. G. Dumoulin

8. **Further Progress in Toxaemia Control.**

By T. F. CORKHILL. *N.Z. med. J.*, **53**, 353–364. Aug. 1954. 34 refs.

Brief statistics of the incidence and mortality of eclampsia in New Zealand are as follows:

Period	Total Births	Cases of Eclampsia	Maternal Deaths	Mortality Rate Per cent
1928–1933	157,264	491 (3·2 per 1,000)	93 (0·6 per 1,000)	18·9
1951–1953	155,766	240 (1·54 per 1,000)	8 (0·05 per 1,000)	3·3

The infant mortality in 1953 was 17 per cent.

The author then proceeds to review the current theories of the causes of the various toxaemias of pregnancy in the light of his own personal obstetric experience. Broadly speaking, he regards the toxaemias of late pregnancy as manifestations of hepatic dysfunction precipitated by a number of causes, such as placental factors, nutritional factors, difficult labour, and pressure. There is defective hormonal control with resultant vaso-spasm leading most frequently to renal dysfunction with salt and water retention, hypertension and albuminuria, but sometimes involving the uterus and the brain. Gross hepatic damage occurs in a small proportion of cases in the form of periportal zonal necrosis, and is probably associated with some element of placental separation.

Preventive treatment based on this hypothesis has had remarkable success. The author regards the two most important steps as being a protective diet with high protein, liberal carbohydrate and adequate vitamin and calcium content; and the utmost vigilance in detecting the first evidence of salt and water retention and immediate counteraction.

L. Woodrow Cox

9. **Toxemia of Pregnancy—ACTH and Cortisone Therapy.**

By R. R. MARGULIS, C. P. HODGKINSON, W. C. RATTAN and J. S. JEWELL. *Amer. J. Obstet. Gynec.*, **67**, 1237–1246. June 1954. 6 tables. 26 refs.

Cortisone and/or ACTH were administered orally, intramuscularly and intravenously to 9 patients with toxaemia of pregnancy. There was no evidence that any were improved by the treatment. Sixteen normal pregnant women were given the same substances for 3 weeks in a total dose of at least 1,000 mg. No signs or symptoms of pregnancy toxaemia were produced in any of them. One of the most striking observations was the increased tolerance of pregnant women to the administration of ACTH and cortisone but the reason for this is unknown.

F. J. Browne

10. **Continuing Vasodilator Infusion Therapy.**

By M. L. MCCALL. *Obstet. and Gynec.*, **4**, 403–410. Oct. 1954. 3 figs. 34 refs.

The author believes that the harmful effects of toxaemia of pregnancy are due to vasospasm. In his studies on the effects of heavy sedation on the brain, he has found that these agents (especially the intravenously administered barbiturates) depress oxygen metabolism of the brain without alleviating the vasospasm. He therefore does not favour the use of heavy sedation in toxaemia. It is believed that the hypertension in pregnancy toxaemia is of humoral and not neurogenic origin so that ganglion-blocking substances are ineffective in treating it. Veratrum viride has been found useful. L-hydrazinophthalazine (Apresoline) is a vasodilator which brings about renal vasodilatation and relieves cerebral spasm. McCall has tried it in toxaemia combined with a mixture of 2 purified alkaloids of veratrum viride called cryptenamine (Unitensen). The substances were given by intravenous infusion in 18 cases with good result. There was an average fall in blood pressure from 190 to 125 mm. Hg systolic and from 118 to 76 mm. Hg diastolic. The infusion was given from 4 to 96 hours. In 7 patients there was a permanent lowering of blood pressure.

J. G. Dumoulin

11. **Similarity of Symptomatology of Premenstrual Syndrome and Toxaemia of Pregnancy and their Response to Progesterone.**

By K. DALTON. *Brit. med. J.*, **2**, 1071–1075. Nov. 6, 1954. 4 figs. 36 refs.

The author, a general practitioner in Edmonton, Middlesex, undertook an investigation to discover the incidence of premenstrual syndrome in those who had previously suffered from toxaemia of pregnancy. She investigated 952 women of whom 237 had suffered from toxaemia of pregnancy. The premenstrual syndrome was only diagnosed when (1) the symptoms were present in each of the 3 previous cycles, (2) sufficiently severe to demand relief by analgesics or the seeking of medical advice and (3) occurring at a specific phase of the cycle —either in the 3 premenstrual days, throughout menstruation, or midcycle.

The diagnosis of toxaemia was limited to those who had a blood pressure of 120/70 mm. Hg or below in early pregnancy, and in whom the pressure rose after the 28th week to 140/90 mm. Hg or more, and for which treatment was given.

Results showed that 86·4 per cent of toxaemic mothers

gave a history of premenstrual syndrome, as against 16·6 per cent of controls. The incidence of premenstrual syndrome increased in toxaemic mothers from 76·6 per cent after one pregnancy to 100 per cent after 4 pregnancies. Of toxaemic mothers 26·2 per cent had the premenstrual syndrome prior to the toxaemic pregnancy. Many of the toxaemic mothers described minor symptoms before the apparent onset of toxaemia very similar to those of the premenstrual syndrome.

Day-to-day observations on several cases of the premenstrual syndrome showed varying degrees of weight gain, oedema, hypertension and albuminuria occurring during the premenstruum. The author notes the special proneness in epileptics to fits at this time.

As it has been shown that the premenstrual syndrome is often relieved by progesterone, a trial of progesterone therapy in toxaemia of pregnancy was undertaken. At routine antenatal visits patients were asked about the presence of nausea, headache, vertigo and lethargy, and if any of these symptoms were present, she was given an immediate injection of progesterone 25–50 mg. If there was immediate relief, she was treated symptomatically by progesterone 10–150 mg. daily on alternate days, or 10–250 mg. daily of ethisterone, dosage being raised until she was symptom-free.

Progesterone gave speedy relief in 34 cases of vomiting of early pregnancy. Ten cases of mild, and one of more severe toxaemia were treated on these principles, and all went to term without bed rest, and without foetal loss. The author feels that failure of previous authors to control cases of toxaemia of pregnancy by progesterone may have been due to the small doses used. She also notes that ethisterone, though more convenient to use, is far more variable than progesterone in the dosage required.

Eileen Wilson

12. Retinal Detachment as a Complication in Toxaemia of Pregnancy.

By P. A. JARVINEN and O. KINNUNEN. *Gynaecologia, Basel*, **138**, 405–409. Sept. 1954. 12 refs.

The author reviews some of the literature on retinal detachment as a complication of late pregnancy. He quotes Dieckmann's description (*Toxemias of pregnancy*, 1952, p. 240) of the eye changes found in toxaemia as follows:

1. The first sign consists in spasm of the retinal arteries or their branches.
2. Oedema, which first sets in above and below the papilla and then spreads along the retinal blood vessels.
3. Appearance of haemorrhage and exudates.
4. Detachment of the retina, usually bilateral, which is an extremely rare complication of toxaemia.

Two cases are described, one a woman of 25 and the other of 26, in which retinal detachment occurred as a complication of severe toxaemia of late pregnancy. In both cases complete recovery of vision took place.

In the discussion, the author quotes observations from the literature showing that blindness occurs as a complication of eclampsia in 1 to 3 per cent of cases. Nine causes of blindness during pregnancy are given as:

1. Central retinal arterial and venous thrombosis.
2. Oedema of the retina.
3. Central disturbance of the visual centre in the occipital lobe or lobes as by oedema or haemorrhage.
4. Detachment of the retina, partial or complete.
5. Disturbance of the optic nerve, i.e. optic neuritis.
6. Psychogenic disturbance.
7. Intracranial venous thrombosis, especially if the sagittal sinus is involved.
8. Retinal ischaemia following repeated severe haemorrhage.
9. Persistent spasm of the retinal vessels.

These are quoted from Carpenter, Kava and Plotkin (*Amer. J. Obstet. Gynec.*, 1953, **66**, 641).

Retinal separation is considered to be an indication for immediate interruption of pregnancy. The time required for recovery varies from 2 days to 2 months but vision is restored well without operation. No special treatment is required except that of the toxaemia.

Josephine Barnes

13. Compartmental Distribution and Shift of Water and Electrolytes in Pre-eclampsia. Part I. Distribution of Electrolytes in the Serum and Oedema Fluid.

By H. J. TATUM. *Amer. J. Obstet. Gynec.*, **67**, 1197–1201. June 1954. 2 tables. 5 refs.

Serum and oedema fluid determinations of sodium, potassium and chlorides were made in normal pregnant women and in patients with pre-eclampsia, all in the last trimester. The mean sodium concentration in the serum of normal pregnant women was 142·3 m.eq. per litre, while in patients with pre-eclampsia it was 137·5, a difference that is highly significant. The mean chloride serum concentration in the non-toxaemic women was 104·3 m.eq. per litre; in the patients with pre-eclampsia it was 101·0, again a highly significant difference. On the other hand there was no significant difference in potassium concentration.

In patients with demonstrable pre-tibial oedema but no toxaemia the mean difference in concentration of sodium in serum and oedema fluid was 0·58 m.eq. per litre, the serum having the higher concentration, but in pre-eclamptic patients the concentration of sodium was higher in the oedema fluid, the mean difference being 2·05 which is highly significant. The concentration of chlorides in the oedema fluids of both groups was consistently greater than that in the serum but the difference was probably not significant. Of potassium, the concentration in the oedema fluids of both groups was consistently less than that of the sera, but the difference was not significant.

It therefore appears that there is a shift of sodium from the vascular to the extra-vascular compartment in pre-eclampsia but there is no justification for assuming that both sodium and chlorides are involved in unionized sodium chloride.

F. J. Browne

14. The Value of Radiology in Ante-partum Haemorrhage.

By J. DAWSON and P. R. MITCHELL. *Brit. med. J.*, **2**, 1085–1086. Nov. 6, 1954. 3 figs. 11 refs.

The authors describe the results obtained in the use of radiography in determining the placental site in cases of ante-partum haemorrhage admitted to the Royal Hampshire County Hospital during 1951–3, and how these results have been applied. The technique used follows that described by Reid and Whitehead, but no special filters were used. The following views were taken: (1) lateral views of the abdomen—one penetrated film for the posterior half of the abdomen and one "soft" film for the anterior half. (2) A lateral view of the pelvis in the erect or semi-erect position. These two views were usually sufficient if the placenta was on the anterior or posterior uterine wall. When mainly on the lateral wall, two further views were taken. (3) Antero-posterior or posterior-anterior films of the abdomen in the erect position; and (4) oblique films of the abdomen in the recumbent position.

The authors note that the placental shadow varied in thickness between 3·1 and 5·8 cm.—the uterine thickness elsewhere being between 0·5 and 1·3 cm. Interpretation of the films was difficult before the thirty-second week, as the foetal subcutaneous fat is insufficient to reveal its outline. It was difficult also with abnormal presentation.

The present practice at this hospital is to discharge home one week after cessation of haemorrhage any patient in whom the placenta has been shown radiologically to be normally implanted, and in whom a speculum examination has excluded cervical or vaginal pathology.

The radiological results were analyzed in 47 cases. Twenty showed placenta praevia, including 4 cases diagnosed before haemorrhage occurred. All these were confirmed at operation. Twenty-four showed normal implantations and had normal deliveries. In 3 cases the radiologist's report was doubtful, and these were subsequently shown to be placenta praevia.

During this period 64 cases were not X-rayed, chiefly because vaginal delivery occurred shortly after admission.

The authors feel that the method is reliable enough to discharge from hospital without vaginal examination patients with an apparently normally situated placenta. They also feel justified on occasion in performing Caesarean section without prior vaginal examination, on the radiologist's report.

Eileen Wilson

15. **Obstetric Shock.**

By C. L. SCHNEIDER. *Obstet. Gynec.*, **4**, 273–294. Sept. 1954. 59 refs.

A recent advance in obstetrics has been the discovery of defibrination of the blood in cases of abruptio placentae and occasionally in eclamptics. In certain mothers who died suddenly of abruptio placentae, evidence has been found of fibrin deposits and emboli suggesting that massive coagulation within the circulating blood was the cause of the apparent disappearance of the fibrinogen. It is thought that, in mothers who survive, fibrin deposits may be formed and then lysed away. The mechanism of the conversion of fibrinogen into fibrin which produces the acquired fibrinopenia in abruptio placentae is discussed in detail by the author. There is considerable evidence that it is due to tissue juices and debris passing into the circulation at the placental site. Many active substances may be liberated here, but most significant is tissue thromboplastin which has been shown to produce similar changes and shock when injected into the circulation of experimental animals. In the initial stages of abruptio placentae a retroplacental haematoma is formed which is fed by an arterial blood supply. The haematoma ruptures and the rupture is back into the maternal circulation. The bleeding in placenta praevia differs in that pressure is not built up in a haematoma since the bleeding involves a passive venous flow into the vagina.

That a similar mechanism exists in the shock caused by amniotic fluid embolism is not proven, and the author believes that the shock is caused by the pulmonary vascular embolic debris producing right heart failure.

After long-standing foetal death *in utero*, symptoms of a bleeding tendency including afibrinogenaemia have been described. These may be due to the release of thromboplastin by degenerating placental tissue adjacent to surviving placenta. Similarly in hydatidiform mole, if there is a high pressure inside the uterus, some portions of the mole may undergo degeneration, necrosis and liquefaction. This liquid and debris may find its way into the circulating blood through still functioning portions of the intervillous lake. Conceivably from placental infarcts active material could similarly pass into the circulation.

Discussing the therapy of abruptio placentae, the author considers that it is dangerous to stimulate the uterus or allow a long labour. Rapid delivery is necessary and he favours the frequent use of Caesarean section and the employment of a blood transfusion. Hysterectomy at the time of section is not indicated.

J. G. Dumoulin

16. **Pregnancy Prognosis Following Repeated Abortion.**

By H. SPEERT. *Amer. J. Obstet. Gynec.*, **68**, 665–673. Aug. 1954. 3 tables. 4 refs.

The author criticizes Malpas's conclusion regarding the probable outcome of pregnancy after 3 spontaneous abortions on the grounds that he did not distinguish between primary and secondary habitual abortion, that he assumed too high a spontaneous abortion rate, namely 18 per cent, and too high a proportion of pregnancies that abort because of a recurrent factor, namely 1 per cent. Speert defines habitual abortion as a succession of 3 or more spontaneous abortions of a foetus of less than 1,000 g. If the weight is not known the diagnosis is based on a gestation of less than 28 weeks.

In the present paper he describes the outcome in 121 such cases, 76 being primary and 45 secondary consecutive abortions. Thirty-four were treated by hormones in varying combinations, and of these 65 per cent carried to viability as compared with 87 per cent of the 87 women who were not treated by hormones. This shows that the good results cannot be credited to hormone therapy.

The prognosis for a viable pregnancy after a succession of 3 or more abortions thus seems to be far better than is

indicated by the estimated 27 per cent (Malpas) or 16 per cent (Eastman). Good results that have been imputed to various therapies are predicated on an unfounded pessimism over pregnancy outcome in the untreated patient.

F. J. Browne

17. **Potassium Permanganate as an Abortifacient.**

By C. C. LINDSAY and C. V. WARD. *Canad. med. Ass. J.*, **71**, 465–467. Nov. 1954. 1 fig. 1 table. 12 refs.

Thirty-seven cases of potassium permanganate burns of the vagina are reported, the drug being used as an abortifacient by 35 women. Five women succeeded in aborting themselves, but the series is considered too small to be of statistical significance. Series are reviewed in which the abortion rate varied from 0–9 per cent, the expected spontaneous abortion rate. Symptoms, physical findings, treatment and complications are described.

O. Schmidt

18. **Note on Afibrinogenaemia in Pregnancy.**

By J. K. FEENEY. *J. Irish med. Ass.*, **36**, 310–312. Oct. 1954.

The author points out that toxic accidental haemorrhage is relatively common in Dublin and accordingly there is ample opportunity to study the problem. In the severer forms of toxic accidental haemorrhage the blood which collects behind the placenta and membranes clots initially but within a short period the available fibrinogen may become seriously depleted or even absent. It is unusual for a case of toxic accidental haemorrhage to show afibrinogenaemia but lesser degrees of fibrinogen depletion are not uncommon.

In the author's experience hypofibrinogenaemia has been encountered under the following circumstances: (1) A hypertensive grand multipara; (2) A toxaemic younger patient; (3) A woman carrying a dead foetus; (4) A patient whose pregnancy, up to the time of the haemorrhage, had been absolutely normal; (5) In 2 cases of vulvo-vaginal haematoma.

Clinical details of two cases admitted on successive nights to the Coombe Hospital are given.

Case I. The patient, a gravida-6, aged 30 years, was admitted to hospital because of an accidental haemorrhage at 28 weeks. She had attended the antenatal clinic and the blood pressure had always been within normal limits. At 24 weeks her blood was noted to contain an incomplete antibody. She was severely shocked on admission and displayed all the features of a severe mixed type of accidental haemorrhage. Schneider's test showed an absence of fibrinogen. Three pints of blood were given but a pernicious trickle of blood continued from the vagina. Two further pints of blood were given but the vaginal trickle continued. The membranes had been ruptured shortly after admission; there had been no response to pitocin. Under a local anaesthetic a lower segment Caesarean section was performed and the macerated foetus and placenta delivered. At the finish of the operation, 6 hours after the patient's admission, a few clots were expelled from the vagina. Bleeding soon ceased and the patient's condition improved. Schneider's test revealed less marked fibrinogen deficiency. The patient was discharged well on the 16th day.

Case II. The patient aged 35 years, a gravida-3, was admitted as an emergency case of toxic accidental haemorrhage at 32 weeks. She suffered from moderate shock and there was a steady trickle of non-clotting blood from the vagina. Schneider's test showed no clot over a period of several hours observation. Despite the transfusion of 2 pints of blood and plasma solids, the vaginal trickle continued. The membranes had been punctured but the uterus had not responded. Three hours after admission a lower segment Caesarean section was performed under a general anaesthetic. Within an hour of the operation all bleeding had ceased. Twelve hours after delivery Schneider's test showed clot at a titre of 1–100. The patient was discharged on the 14th day.

The author concludes by stressing the need for improvement in the standard of antenatal care given to patients. In selected cases, he believes that induction of labour and occasionally Caesarean section will forestall accidental haemorrhage and save babies.

For severe cases of accidental haemorrhage where there is severe bleeding and impending renal failure Dr. Feeney suggests a plan of treatment embodying 14 points. Interested readers are referred to the original article for details of the author's management of these cases.

J. K. Russell

19. **Leukaemia and Pregnancy.**

By J. ALLAN. *Brit. med. J.*, **2**, 1080–1082. Nov. 6, 1954. 2 tables. 15 refs.

The author from the Western Infirmary, Glasgow, reviews the world literature in 95 cases of leukaemia and pregnancy and describes 4 more cases. The first case described was that of chronic myeloid leukaemia, treated by urethane prior to pregnancy. She carried to term, but had a stillbirth associated with placenta praevia. She needed massive transfusions during the puerperium to combat haemorrhage. She responded temporarily to a second course of urethane but died about 6 months later.

A second case of chronic myeloid leukaemia had been treated by X-rays prior to the onset of pregnancy. She carried to term, the child was born alive and there was no post-partum haemorrhage, but progressive anaemia caused death on the 25th day after delivery.

A third case of chronic myeloid leukaemia was diagnosed at the 33rd week of pregnancy. She went into labour at the 37th week. The child was born alive, but the mother died of post-partum haemorrhage.

The fourth case, also of chronic myeloid leukaemia was diagnosed at necropsy in a patient who died on the fourth day of the puerperium after a premature twin delivery.

In commenting on the world literature, the author notes that 61 per cent of the total 95 cases were of chronic myeloid leukaemia. Thirty-four cases of acute leukaemia have been reported, with a maternal mortality of 100 per cent. The author concludes that termination of pregnancy is not justified here, unless to secure a living child. Most patients survived pregnancy in chronic leukaemia, and post-partum haemorrhage was not so frequent a com-

plication as hitherto thought. The author considers that in most cases the danger of interruption of pregnancy is as great as that of parturition. The foetal loss is chiefly due to prematurity.

Eileen Wilson

20. The Relation of Pregnancy to Abnormalities of the Cervical Epithelium.

By B. PECKHAM, R. GREEN, J. T. CHUNG, M. A. BAYLY and H. B. W. BENARON. *Surg. Gynec. Obstet.*, **99**, 401–412. Oct. 1954. 13 figs. 9 refs.

During the course of a study at the Chicago Maternity Center concerned with the cervix during pregnancy and the post-partum period, the authors have encountered, in 19 patients, epithelial abnormalities which are not pre-invasive cancer. Most of these were found in biopsies taken because of a previous atypical or positive cytological smear or because of gross cervical abnormalities.

The epithelial abnormalities are divided into equivocal lesions and atypical basal cell hyperplasias. In the equivocal lesions the nuclear atypia, though extending through the full thickness of the epithelium, is less marked in the superficial layers, than is observed in well-differentiated pre-invasive carcinoma. In the atypical basal cell hyperplasias the abnormalities do not extend throughout the thickness of the epithelium and the cells and nuclei of the superficial layers appear normal.

The authors set out to show that these lesions are not evanescent pregnancy changes since most of them have persisted well beyond the termination of pregnancy.

Five cases of atypical basal cell hyperplasia during pregnancy are described and in 4 of these the lesion persisted or progressed following delivery. The apparent rarity of this condition is believed to be due to the method of selection of patients for biopsy and the lesion is apparently more common than either equivocal lesions or pre-invasive carcinoma when the patients biopsied are unselected.

In the 14 instances of equivocal lesions the abnormality disappeared following delivery in 5, regressed to basal cell hyperplasia in 2 and persisted in 7.

[In the text the authors point out that most publications dealing with histological changes in the cervix during pregnancy fail to compare the data with the findings in a comparable group of non-pregnant women. Their own communication suffers from the same omission and one feels that the contention, that these lesions are incidental findings during pregnancy, would be strengthened greatly if a like incidence was demonstrated entirely apart from pregnancy in a similar group of women.]

John P. Erskine

21. Urinary Pregnanediol and Difficulties of Renal Permeability. A Study of 25 Cases of Chronic Nephritis Complicating Pregnancy. (Prégnandiol urinaire et troubles de la pérmeabilité rénale. Étude portant sur 25 cas de néphrites chroniques compliquées de grossesse.)

By H. PIGEAUD, R. BURTHIAULT and R. BETHOUX. *Gynéc. Obstét.*, **53**, 417–427. 1954.

The study of these cases confirms the classical teaching on the subject. Chronic nephritis in pregnancy not complicated by hypertension holds an equally good prognosis for mother and child.

Eight mothers were carefully followed until their deliveries: 6 were confined at term of living children of average weight, and 2 had premature confinements induced at 8 months, both giving birth to living children.

Chronic nephritis cases, on the other hand, complicated by hypertension had a guarded prognosis both for mother and child.

In the case of 9 mothers who were followed up till their confinements, 7 children either died during the antenatal period, or during delivery or in the first 48 hours after birth. Only 2 children were born alive and they were less than average weight.

D. Maxwell

22. Foetal Defects following Insulin Coma Therapy in Early Pregnancy.

By I. G. WICKES. *Brit. med. J.*, **2**, 1029–1030. Oct. 30, 1954. 14 refs.

Duraiswami has described the production of skeletal and ocular defects by injecting insulin at an early stage of development of the chick embryo. Oakley has found a high incidence of foetal abnormalities where the mother was diabetic though he could not correlate this with hypoglycaemia.

A case is described which seems to lend support to the suggestion that foetal defects may be associated with high insulin levels in early pregnancy. She was a schizophrenic who was given 35 insulin comas and one general convulsion between 12th October and 3rd December and was delivered at the end of the following April, apparently 4 weeks prematurely, of a 6 pound 4 ounce infant who was later diagnosed to be suffering from mental deficiency with hyperteleorism and optic atrophy.

A search for reports of other cases where insulin coma therapy and pregnancy have coincided revealed only 7 additional ones. Study of these cases supported the idea that such therapy might be harmful to the foetus before the 10th week of pregnancy, though, with 1 spontaneous and 1 therapeutic abortion and 1 normal baby following therapy at the 10th week, it was difficult to be dogmatic.

Doreen Daley

LABOUR

23. The Influence of Light and Darkness on the Clinical Onset of Labour. (Der Einfluss des Lichtes und der Dunkelheit auf den klinischen Geburtsbeginn.)

By J. MALEK. *Gynaecologia, Basel*, **138**, 401–405. Sept. 1954. 8 refs.

The author studied the time of onset of labour in 92,590 labours. Of these, 23,765 began with rupture of the membranes and 68,825 with the onset of painful uterine contractions.

In a study of 69,995 births it was found that 1·5 more labours began during the hours of darkness, that is between sunset and sunrise, irrespective of the season than during daylight. These figures were arrived at by an analysis of the number of labours which started during

any one hour of the day or night. The average is approximately the same in all seasons.

Josephine Barnes

24. **The Influence of Posture and of Changes in Posture on Uterine Activity during Labour.** (Der Einfluss der Korperlage und des Lagewechsels auf die Wehentätigkeit.)

By S. LORAND and T. POGANY. *Gynaecologia, Basel*, **138**, 374–382. Sept. 1954. 5 refs.

Lorand's tokoergometer has been used to study the activity of the uterus during labour in 385 women. The effects of posture on the course of labour were studied and contrary to the usually accepted view it was found that the recumbent posture is more advantageous for an increase in uterine activity. A study was made of labour in 240 primigravidae with intact membranes. A spontaneous increase in uterine activity is noted in early labour but this is independent of posture though slightly increased when posture is changed, as from lying to standing. In uterine inertia, the recumbent position led to the greatest increase in activity. The authors point out that spontaneous decreases in uterine activity are frequent in the course of normal labour and this fact should be taken into account in assessing the effects of analgesic drugs.

Josephine Barnes

25. **The Management of Labour in Contracted Pelvis.**

By H. MACLENNAN. *Brit. med. J.*, **2**, 837–840. Oct. 9, 1954. 4 figs. 10 refs.

The author discusses the fall of incidence of contracted pelvis in the Royal Maternity and Women's Hospital, Glasgow, from 27 per cent of admissions in 1903, to 9 per cent in 1928 and 4 per cent at the present day. There has been a corresponding improvement in the degree of contraction from the lowered incidence of severe rickets, but there is still a high incidence of minor contraction. In all cases under discussion the true conjugate was only 10 cm. or less.

The author traces the changing trends of treatment—from craniotomy and classical Caesarean section in 1903—to the lower segment operation or forceps delivery in 1953. He now puts in a plea for the trial of induction of labour in these borderline cases. His present method is surgical induction when the baby's weight would appear to be about 6 pounds, and the pelvic contraction of only minor degree. He feels that with antibiotic cover there is little risk if Caesarean section is ultimately needed.

Operation may prove necessary at any time following induction, especially for foetal distress or inertia. By the proper use of trial induction, the author hopes to avoid the unnecessary elective section on one hand, or the difficult forceps extraction on the other.

Eileen Wilson

26. **Induction of Labour.**

By F. A. BELLINGHAM. *Med. J. Aust.*, **2**, 545–548. Oct. 2, 1954.

A series of figures from The Women's Hospital, Crown Street, Sydney, embracing the years 1950–1951 and 1952–1953, July to June in each case are studied. In these periods 9,255 viable infants were born at the hospital and 3·4 per cent of the mothers had labour induced by artificial rupture of the membranes.

In approximately 45 per cent previous attempts at induction by medical means had failed and in approximately 58 per cent medical means were used to augment the effect of rupturing the membranes. On the average, medication was given 12 hours after the membranes had been ruptured. The incidence of artificial rupture of the membranes was nearly equal in primiparae and multiparae.

Factors favouring success were the presence of the so-called ripe cervix, and engagement of the head in a primipara.

Low rupture of the membranes was more efficient than high, and primigravidae respond better than multiparae.

In the series of 321 cases the indications were as follows: pre-eclamptic toxaemia 253, Rh-negative mother with agglutinins 20, ante-partum haemorrhage 14, diabetes mellitus 8, cardiac disease 5, pyelitis 5, chronic nephritis 5, hydramnios 4, post-maturity 3, haematuria 1, acute bronchitis 1, epilepsy 1, hysteria 1.

In the series there was no maternal death. There were 14 stillbirths or neonatal deaths including 3 which were inevitable with anencephalic and hydrocephalic infants and hydrops. The corrected foetal mortality was 3·4 per cent.

In only 1 case was the neonatal death directly due to the induction. Prolapse of the cord did not occur.

S. Devenish Meares

27. **Surgical Induction of Labour in Modern Obstetric Practice.**

By R. A. TENNENT and M. D. BLACK. *Brit. med. J.*, **2**, 833–837. Oct. 9, 1954. 7 figs. 12 refs.

The authors reviewed cases in which surgical induction of labour was performed, from 1950 to 1952 inclusive, in the maternity units at the County of Lanark Maternity Hospital, Bellshill, and the William Smellie Memorial Hospital, Lanark. The authors were directly responsible for the care of these patients, which totalled 1,585 cases, representing 18·3 per cent of all deliveries for that period. Thirty-one cases of ante-partum haemorrhage were not included, because of the difficulty of determining the time of onset of labour and the effect of surgical induction alone on the foetus.

The method was rupture of the membranes, either with a male metal catheter, or a Drew Smythe catheter. Either the forewaters or hindwaters were ruptured, and no regard was paid to the condition of the cervix, or position of the head. The main indications were post-maturity and hypertensive toxaemia, but 121 cases of contracted pelvis were included. Of the primigravidae 74·8 per cent and of the multiparae 72·5 per cent were in labour within 24 hours. The figures for those in labour within 72 hours were 91 per cent and 88 per cent. Failures (over 72 hours) were 9 per cent and 12 per cent respectively.

It is the authors' policy to induce labour when the patient is apparently one week postmature. In this

series of 633 cases, the corrected foetal mortality was 0·9 per cent. Of the infants 35·1 per cent weighed over 8 pounds. Labour lasted over 48 hours in only 1·3 per cent. The forceps rate was 7·1 per cent. The Caesarean section rate was 1·1 per cent. Foetal distress was noted 20 times in the primigravidae, and 4 times in the multiparae.

Labour was induced for toxaemia in 504 cases—either for advanced and persisting toxaemia, or because the patient had reached 38 weeks. The corrected foetal mortality was 4·1 per cent. 10·9 per cent were not in labour after 72 hours. The forceps delivery rate was 10·5 per cent—the Caesarean section rate 3·5 per cent. Foetal distress was noted 29 times.

Surgical induction was performed in 121 cases of contracted pelvis—53 primigravidae and 68 multiparae. The 38th week was the chosen time, and carried out on only minor cases of pelvic contraction. The corrected foetal mortality was 1·7 per cent. Prolonged labour was infrequent. 11·6 per cent of cases required forceps. The Caesarean section rate was 9·9 per cent.

Inaccurate estimation of the infants' weight was a serious disadvantage, and in 5 cases the weight was under 5 pounds.

Induction was performed at 38 weeks in 39 patients who had had a previous Caesarean section. There was 1 maternal death from paralytic ileus in which Caesarean section was performed for foetal distress. Forceps were applied as a routine in the second stage.

Forty-five patients required Caesarean section after surgical induction of labour. There were no cases of frank sepsis—antibiotics were usually given prophylactically.

A period of over 72 hours' induction-labour interval was noted in 166 cases. Low-grade pyrexia followed in 79 cases, but only in one did it rise above 100°. The corrected foetal mortality was 5·4 per cent. The authors feel that the more frequent use of surgical induction has contributed to a low foetal mortality without maternal risk, but stress the need for a more efficient method of induction to eliminate the prolonged latent period.

Eileen Wilson

28. **Methergen in the Conduct of Delivery.** (La méthylergobasine (méthergin) dans la conduite de la délivrance.)

By F. CHARVET and A. LA SELVE. *Gynéc. Obstét.*, **53**, 515–524. 1954. 2 refs. (Bibliography in Thesis by A. La Selve, University of Lyon, 1953.)

Methergen in the opinion of the writers is a powerful oxytocic, the use of which, following a certain technique, has given excellent results in the course of delivery.

The intravenous injection of one ampoule of Methergen given after the birth of the head, and before the delivery of the shoulders, results in a strong, practically painless, contraction of the uterus which causes almost immediate separation of the placenta. After several minutes it is possible to determine that the placenta has separated by the softening of the uterus and lengthening of the umbilical cord. Manual compression of this contracted uterus, provided the clinical signs of separation are present, i.e., rising up of the uterus, and diminution in its transverse diameter, results in birth of the placenta in 90·8 per cent of cases with a loss of blood well within normal limits and averaging 300 ml. It was also the writers' experience that a second injection was justified if the patient had to have general (particularly ether) anaesthesia, or if there was a tendency to bleeding after the delivery of the placenta. The use of this drug was found particularly beneficial if, owing to anaesthesia, there was a fear of post-partum haemorrhage, or if there was an indication for a rapid delivery and in particular in anaesthetized women after forceps delivery.

D. Maxwell

29. *"**Controlled Labour." Pitocin Drip with or without Associated Drugs.** (Accouchement dirigé. La perfusion d'extrait post-hypophysaire associée ou non à d'autres médications.)

By R. ROUCHY and J. F. BREIL. *Gynéc. Obstét.*, **53**, 364–374. 1954.

During 1952 the writers dealt with 289 confinements treated with pitocin drips with or without associated drugs. They arranged their cases in the following groups.

1. *Normal Obstetric Conditions*

A. Intravenous drips of Pitocin only. Here there were 101 cases, 48 of which were primigravidae and 53 multiparae.
B. Intravenous drips of Pitocin plus Spasmalgin: 97 cases, 45 primigravidae and 52 multiparae.
C. Intravenous drips of Pitocin plus Phenergan: 27 cases, 9 primigravidae and 18 multiparae.
D. Intravenous drips of Pitocin plus Spasmalgin and Phenergan: 34 cases, 21 primigravidae and 13 multiparae.

The writers concluded that the course of normal labour was not particularly altered by these drugs.

2. *Specific Obstetric Conditions*

A. Breech presentation: 20 cases, 8 primigravidae and 12 multiparae.
B. Anomalies of the dynamic uterus.
C. Certain minor degrees of contracted pelvis.
D. Twins.

They concluded it was difficult to assess the value of these drugs in labour as the factors concerned varied so much from one woman to the other. On the other hand they consider there is a place for the term "accouchement dirigé", that is "controlled labour" and by this term they include the idea of regulation and speed of a labour.

The writers are well aware of, and refer to, the dangers of Pitocin drips.

They appreciate the value of a triple basal medication in the form of phenergan+dolosal+largactil which in their opinion reduces spasm of the uterus—but above all the addition of analgesia. The pitocin drip they would look upon only as an adjunct for regulating the pace of the labour.

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*[Translators' note:—The term "accouchement dirigé" is better not translated at all, as it is essentially a French idea—and is best to enter the English technical obstetrical vocabulary as such.]

They distinguish two types of women:

(1) Those who have been regularly seen at the antenatal clinic by the accoucheur and on whom satisfactory psychotherapy can be applied. In this series there were 63 cases, 26 of which (14 were primigravidae and 12 multiparae) only had the triple basal medication. Labour averaged 9 hours in the primigravidae and 6¼ hours in the multiparae. Trilene superimposed on the basal medication rendered low forceps easy.

(2) The second category concerns nervous apprehensive types not supervised antenatally by the accoucheur or his team, often admitted after a fairly long labour with badly arranged sedation. Thirty-six such cases are described, 20 primigravidae and 16 multiparae.

The writers finally conclude that it is essential to adapt their regime to the individual case, as regards dosage, method of administration and timing.

Further a minute analysis of the clinical signs is required to include pelvic anatomy, study of the soft parts, as well as the study of commencing foetal distress and any abnormal physiological action of the uterus.

D Maxwell

30. **Occiput Posterior Position.**

By D. M. Haynes. *J. Amer. med. Ass.*, **156**, 494–496. Oct. 2, 1954. 2 refs.

This report presents data from 360 cases in which foetuses weighing 1,500 g. or more were found to be presenting in the occipito-posterior position during labour. The cases represent 2·9 per cent of 12,488 cephalic births delivered at Parkland Hospital, University of Texas, during a 6-year period. The author is concerned largely with the persistent occipito-posterior, and the fact that 324 cases were delivered as such indicates that the posterior position was rarely diagnosed early in labour, so that figures for spontaneous anterior rotation are not given.

Sixty cases were primigravidae and 300 were multigravidae. The method of delivery was spontaneous (almost all of these with the occiput directly posterior) in 59·2 per cent, low forceps in 28·3 per cent, and mid-forceps in 12·5 per cent. The frequency of mid-forceps operations has dropped steadily as the recognition of cephalo-pelvic disproportion has improved. There was no maternal death, and injury to maternal soft tissues occurred in 11·4 per cent. The total gross foetal mortality was 4·7 per cent (corrected, 3·9 per cent).

The Staff of the Parkland Hospital believe that after the foetal head has become moulded in the posterior position it is far more likely to be damaged by anterior than by posterior rotation, especially if the operator is inexperienced. If an obliquely posterior position persists after 45 minutes in the second stage and manual rotation cannot be easily performed, low forceps rotation to occiput directly posterior is carried out followed by prompt delivery after episiotomy. The author recommends this method for residents in training and believes that the occipito-posterior position, whether persistent or not, ought not to be considered as implying an abnormal mechanism of labour. [It is difficult to reconcile this teaching with the fact that failure to recognize and to rotate a persistent occipito-posterior to the anterior position is still a common cause of "failed forceps" by the inexperienced.]

D. W. James

31. **Ergometrine and the Third Stage of Labour.**

By L. W. Cox. *N.Z. med. J.*, **53**, 380–387. Aug. 1954. 2 figs. 3 tables. 9 refs.

Haemorrhage is still a major factor in the maternal mortality of New Zealand. In 1950, 17·5 per cent of maternal deaths were due to third stage haemorrhage. In that year the crude maternal death rate for complications of the third stage was nearly 3 times higher than the rate for England and Wales. A possible reason for this is the less effective blood transfusion service due to the scattered nature of the population in New Zealand.

The author considers the physiology of the third stage, and discusses the abnormalities that occur. He divides cases into two groups: those following a normal labour where a normal third stage can be expected; and those where the third stage is potentially abnormal. These latter cases follow prolonged labour, incoordinate uterine action, deep anaesthesia, and faulty handling of the uterus by the attendant in the course of delivery.

The use of intravenous ergometrine is recommended for the "potentially abnormal" third stage cases; and a series of 5,250 cases at the Liverpool Maternity Hospital is recorded. In 1900 "potentially abnormal" cases that received ergometrine, bleeding of 20 ounces and over occurred in 0·3 per cent. In 3,350 cases not receiving ergometrine (the remaining deliveries, mainly normal), bleeding occurred in 1·5 per cent of cases. It is suggested that these results reiterate the value of ergometrine intravenously, previously reported by Lister (*J. Obstet. Gynaec. Brit. Emp.*, **57**, 210) and also show the value of careful management of the third stage in normal cases.

Author's Abstract

32. **The Post-partum Bladder.**

By J. W. Funnell, A. H. Klawans and T. L. C. Cottrell. *Amer. J. Obstet. Gynec.*, **67**, 1249–1255. June 1954. 5 figs. 4 refs.

This is a report on the cystoscopic examination of 71 women, 28 of them primiparae, immediately after delivery; 54 of them delivered spontaneously, 13 were delivered by forceps, and there were 3 Caesarean sections. Most of the patients had episiotomy. Normally the post-partum bladder shows only vascular engorgement and the mucosa is of a deeper colour than in the non-pregnant woman owing to dilatation of blood vessels. The longer the labour the greater is the evidence of vesical trauma and this is apt to be especially evident after mid-forceps delivery, and forceps rotation. In such there may be large plaque-like areas of submucosal haemorrhage, with capillary oozing into the bladder cavity, and this may cause gross haematuria. In addition there is marked oedema in the lower bladder area and the region around and between the ureteric orifices.

Re-examination 48 to 72 hours after delivery showed that the changes regress rapidly, but the possibility of

pressure necrosis and fistula formation should be kept in mind in weighing the indications for Caesarean section in prolonged labour.

F. J. Browne

LACTATION

33. Clinical and Chemical Studies in Human Lactation. VIII. Relationship of the Age, Physique, and Nutritional Status of the Mother to the Yield and Composition of her Milk.

By F. E. HYTTEN. *Brit. med. J.*, **2**, 844–845. Oct. 9, 1954. 2 figs. 17 refs.

The author, from the midwifery department, University of Aberdeen, sought to determine the relationship of lactation to age, height, general health, net weight change during pregnancy, and diet during pregnancy in a group of 155 primiparae. At the first visit the general health and physique were assessed and graded on a five-point scale by the senior obstetrician from "excellent" to "very poor". The net weight change is the difference between the postnatal weight, and that at, or before, the 14th week of pregnancy. In 55 cases individual diet surveys were made by weighing total food intake for a week during the seventh month of pregnancy. Milk samples were taken, as previously described, on the seventh post-partum day.

The milk yield was negatively correlated with the age of the mother. It was also negatively correlated with the net weight gain. None of the major constituents of milk was related either to age or weight change. There was a trend to higher yield and fat content in women of good height and physique, but the figures were not statistically significant in the small numbers studied. No correlation was found between milk yield and composition, and the mother's diet.

Eileen Wilson

34. A Bacteriologic and Clinical Study of Breast Abscess.

By C. D. SAWYER and P. H. WALKER. *Surg. Gynec. Obstet.*, **99**, 368–372. Sept. 1954. 3 figs. 4 refs.

This article consists of a clinical and bacteriological review of breast abscess from the Surgical and Bacteriological Departments of the Methodist Hospital, Brooklyn, New York, for the period ranging from 1948–1953.

Early in the series it was noted that penicillin resistance was common among strains of *Staphylococcus aureus* isolated from breast abscesses. A study was, therefore, commenced to determine the effectiveness of various antibiotics with strains isolated from breast abscesses as compared with strains from other sources. Detailed bacteriological investigation was carried out in 50 cases of breast abscess and in 50 cases of staphylococcal infection in other sites. In the former group in only 4 cases was the organism penicillin sensitive as compared with 17 of the latter. In all the breast infections the organisms were sensitive to terramycin, aureomycin, chloromycetin and bacitracin. On bacteriophage typing practically all of the staphylococci from the breast abscesses were found to be phage type III sub-type 52A, while the miscellaneous group proved to be a much more heterogeneous one.

In the prophylaxis of breast abscess the authors recommend terramycin or aureomycin and they have found that, if used early and vigorously, the most severe infections can be completely aborted. It is believed that local treatment is of little value and that the continuance or the discontinuance of breast feeding has no proved worth to either the mother or the baby. The prevention of engorgement with oestrogens is favoured and adequate support of the breast is advised.

When surgery is required an incision should be made around the areola of the nipple through the skin and subcutaneous tissue, but not entering into the ducts. By blunt dissection with a haemostat the affected compartments of the breast are entered. In this way long disfiguring radial incision is avoided and the likelihood of secondary infection is reduced.

John P. Erskine

INFANT

35. High Oxygen and Hyaline-like Membranes.

By P. D. BRUNS and L. V. SHIELDS. *Amer. J. Obstet. Gynec.*, **67**, 1224–1235. June 1954. 5 figs. 2 tables. 16 refs.

The authors produced pulmonary hyaline membrane in 75 per cent of guinea pigs by exposing them in a sealed plastic chamber to 98 per cent oxygen at sea level pressure for 40 to 100 hours. Histological studies showed that the membrane was due to epithelial degeneration, and comparison with post-mortem lungs of infants suggested that the latter have a similar origin. If the animal survived the membrane disappeared without permanent lung damage. Their explanation for hyaline membrane is as follows: "Certain extrinsic factors like maternal disease and obstetrical complications may cause the onset of premature labor. A predisposing factor of fetal anoxia in pregnancy, labor or delivery increased capillary fragility. A precipitating factor, extra-uterine respiration, initiates the bronchiolar and alveolar duct injury with resultant hyaline membrane formation. Aggravating factors, principally immaturity, but also high oxygen, fetal disease or injury, and possibly high steroid levels further enhance pulmonary epithelial and capillary injury."

It is not claimed that high concentrations of oxygen are the sole cause of hyaline membrane but they can be an aggravating factor that may enhance pulmonary damage to the premature infant.

F. J. Browne

OBSTETRIC OPERATIONS

36. An Improved Local Anaesthetic for Minor Obstetric Operations. (Blocco dei nervi pudendi con assocazione di novocaina, adrenalina e jaluronidasi in ostetricia.)

By A. MASSANO and S. MONTICELLI. *Minerva ginec. (Torino)*, **6**, 641–644. Sept. 30, 1954. 1 table. 8 refs.

Local anaesthetics are often used to anaesthetize the area of supply of the pudendal nerves for low forceps operations and for episiotomies, episiorrhaphies and

repairs to the torn perineum. The usual objections to the method are that it causes a local oedema which renders the tissues unduly friable and less easily repaired, that it often fails to relieve pain and that it may be too slow in taking effect.

The method proposed involves the addition of a phial of hyaluronidase (250 V.U.) to every 30–40 c.cm. of the standard 1 per cent novocaine (to every 10 c.cm. of which the usual addition of 15 drops of 1–1,000 adrenalin has been made).

After raising an intradermal "button" in the centre of the perineum, a needle 10 cm. long is pushed up to near the ischial spines and 10 c.cm. of the solution is injected on each side whilst withdrawing the needle. A further 5 c.cm. is similarly injected along the medial edge of each labium, and 5 c.cm. in the middle line of the posterior vaginal wall. Thus 35 c.cm. suffice for each case.

The effect of the hyaluronidase is that the solution diffuses rapidly and the anaesthetic effect is much accelerated and widened, and no oedema is encountered as a result. The authors express themselves as very well satisfied with the procedure, though some women feel it up to themselves to "*si lamentare in modo clamoroso*" whatever is done or not done!

W. C. Spackman

37. **Forceps Delivery of the Aftercoming Head.**

By E. I. Ostry. *Lancet*, **2**, 896–897, Oct. 30, 1954. 6 figs.

The author describes the usual method of applying forceps to the aftercoming head during a breech delivery, in which the trunk of the infant is first lifted upwards towards the mother's abdomen. It is maintained that this does not promote flexion of the head. To overcome this it is suggested that the baby's trunk should be allowed to hang and the forceps then applied to the head. The handles of the forceps are situated behind the baby's trunk which is supported with the left hand while the right is used to operate the forceps. It is suggested that this application accentuates flexion of the head.

H. H. Fouracre Barns

38. **Complete Perineal Laceration.**

By S. A. Fish. *West. J. Surg. Obstet. Gynec.*, **62**, 577–581. Nov. 1954. 4 figs. 3 refs.

After reviewing the aetiology, the author (from the University of Texas) describes methods of operation. For immediate repair the rectal wall is sutured with atraumatic chromic catgut, inverting the mucosa into the rectal lumen; the sphincter is reunited and the remainder of the tear repaired in the usual fashion. A low residue diet is helpful but no specific effort to prevent bowel movements is necessary. Intestinal antibiotics probably add little to the outcome. If conditions are unsuitable for immediate repair it may be postponed until the 10th day of the puerperium. Local cleansing and intestinal antibiotics are advisable and, after curetting all granulation tissue, an anatomical approximation is performed with chromic catgut. The repair of old tears sometimes offers difficulties; it is helpful to give oestrogens for a few weeks to post-menopausal patients and sulphasuxidine is recommended as an antibiotic as it has a mild laxative effect. Three methods of repair are considered but in all it is important to dissect widely, to secure haemostasis and to avoid tension:

1. Layer method: this is similar to the repair of a fresh tear and, after dissection and suture of the rectal wall, sutures are placed in the levatores ani to relieve tension on the sphincter.

2. Warren flap method: a flap of vaginal mucosa is mobilized and brought down over the rectal defect; this lengthens the bowel without leaving a suture line in the rectal canal after the sphincter is joined.

3. Noble method: the anterior wall of the rectum is mobilized and drawn downwards to lengthen the core over which the perineum is repaired. This method is useful for the repair of recto-vaginal fistulae.

All patients are placed on a low residue diet for 5–7 days and some given sulphasuxidine starting on the 2nd post-operative day. A vaginal pack may be used for the first 24 hours. Early ambulation and bathing are encouraged. Perineal pain is controlled with codein and surface anaesthetics and, if there is much oedema, local injection of hyaluronidase gives immediate relief. Complications are rare.

Over 10 years 32 fresh tears and 24 old ones were treated. One new tear broke down and 5 old ones had local sepsis. One patient died from haemorrhage after destruction of the operation site by cutaneous amoebiasis. All but 1 had functionally good results and vaginal delivery was allowed in all patients who subsequently became pregnant.

D. C. A. Bevis

39. **Twenty Years' Experience of Caesarean Section. Analysis of 447 Consecutive Cases from the Service of Professor Weymeersch, 1933–1935 and from the Service of Professor Snoeck, 1936–1952.** (Vingt ans de césarienne abdominale: analyse statistique de 447 cas de césariennes abdominales consécutives, pratiquées à l'Hospice de la Maternité et à la Maternité Universitaire de l'Hôpital Saint-Pierre.)

By P. Piraux. *Gynéc. Obstét.*, **53**, 428–464. 1954. 7 figs. 14 tables.

This is a long and complicated analysis with numerous tables and statistics.

The writer concludes as follows:

1. The incidence of Caesarean section has a tendency to increase in the last few years.

One important reason for this is the giving up entirely of high forceps deliveries and the results are equally better for mother and child.

2. Vaginal delivery is possible in selected women who have had a previous Caesarean section.

Subsequent delivery following Caesarean section for disproportion is possible by the vaginal route provided the baby is of lighter weight than the previous one.

A normal confinement is equally possible when Caesarean section has been carried out for a non-persisting cause such as a breech presentation or placenta praevia.

3. Two-thirds of the operations were performed after the onset of labour or after trial labour.

4. Pelvic disproportion and functional dystocia, singly or combined, were the commonest indications.

5. The total maternal mortality was 2 per cent.

6. The febrile maternal morbidity, in the 20 years, was 37·5 per cent. The use of prophylactic penicillin has reduced the incidence of endometritis but has not reduced the percentage figures for phlebitis.

7. The foetal mortality was 7·37 per cent.

8. Spinal anaesthesia was used as a routine except when contra-indicated and occasionally local anaesthesia was employed.

9. Almost always the lower segment operation was carried out using a transverse incision in the uterus.

10. Sterilization was performed in about 16 per cent of the patients. The commoner indications for this were social rather than medical reasons.

D. Maxwell

GYNAECOLOGY

40. Exfoliative Dermatitis after Acetarsol Vaginal Pessaries.

By B. J. PECK. *Brit. med. J.*, **2**, 850–851. Oct. 9, 1954. 5 refs.

The author describes a case of exfoliative dermatitis following the use of acetarsol vaginal pessaries. The patient inserted two pessaries nightly for a total of 20 days, and then developed a maculopapular eruption, rapidly followed by acute exfoliative dermatitis. Further toxic effects followed dimercaprol injections, but she recovered rapidly after ¼ per cent argyrol in calamine liniment applications.

The author feels that in this case treatment in the first two weeks constituted the sensitizing doses and resumption after menstruation the precipitating dose of a drug-hypersensitivity reaction. Itching during treatment is a signal for immediately stopping treatment.

Eileen Wilson

41. Menstrual Irregularities with Phthisis. (Alteraciones menstruales y tuberculosis pulmonar.)

By G. DI PAOLA. *Obstet. Ginec. lat.-amer.*, **12**, 142–146. May 1954. 8 refs.

The author presents a survey of a series of cases who attended his gynaecological clinic in Buenos Aires complaining of amenorrhoea, and on examination were found to be suffering from phthisis. As a result of the observations made, it is stated that phthisis is a general illness causing physiological alterations in the endocrine glands, especially functional disorders of the ovaries, which cause anomalies of the menstrual cycle. It is also claimed that ovarian function influences phthisis. Cases of genital tuberculosis were not included in the survey. The author presents his observations under three headings.

1. Phthisis and menstrual anomalies. In those cases where the histology of the ovaries could be studied, sclerocystic disease was found and considered to be the cause of the menstrual irregularities. Amenorrhoea was found to be the commonest disturbance and showed itself in early cases of phthisis in 20 per cent, during the period of activity in 50 per cent and in only 4 per cent when the lung disease was recovering.

The author considers that at first the Graafian follicle fails to mature, producing monophasic cycles only, and that later insufficient production of oestrogens due to failure of the anterior lobe of the pituitary gland causes amenorrhoea. He supposes that food deficiency preceding phthisis deprives the pituitary gland of essential requirements, particularly proteins.

2. Repercussions of menstruation on phthisis. The author quotes Sabourin, who states that some tuberculous women die on account of menstruation: indeed the phthisical lesion is said to be worse during menstruation, and an observation in support of this is the increased incidence of haemoptysis during the menses. Conversely, suppression of menstruation reduces the frequency of haemoptysis in such cases. The author has observed that in phthisis there may be a 0·5° premenstrual rise of temperature: he also states that a rise in the B.S.R. after menstruation is a sign of exacerbation of the disease.

3. Tuberculous endometritis and amenorrhoea. This is stated to be one form of latent tuberculosis: histologically two types are described: (*a*) follicular type in which the endometrium functions normally, (*b*) caseous type. In the former type, the menses are usually found to be normal and the condition is only discovered on investigation of sterility: occasionally amenorrhoea is found, and the author demonstrates that this is due to ovarian dysfunction by giving stimulating doses of X-rays. In the caseous type, amenorrhoea exists because of endometrial destruction.

Twenty cases of tuberculous endometritis are mentioned who have never suffered from phthisis, but in 70 per cent of them tuberculous antecedents could be found. Finally, Bush is quoted, who performed 409 autopsies on women who had died of phthisis, and found evidence of genital tuberculosis in only 21 of these: 7 were the caseous type of endometritis.

The author concludes by stating that amenorrhoea in phthisis should be treated by attention to the lung disease, and not by ovarian endocrine therapy.

John F. Foulkes

42. Functional Uterine Bleeding.

By E. G. HOLMSTROM. *J. Amer. med. Ass.*, **156**, 580–582. Oct. 9, 1954.

The most commonly encountered hormone disturbance of the normal pituitary-ovarian-endometrial relationship is that which results in anovulatory bleeding. Although the exact hormone stimulus that initiates ovulation is not well understood it is likely that it occurs when an optimal ratio has been reached between the secretion of F.S.H. and L.H. Anovulatory cycles may therefore result from an imbalance between the secretion of these two hormones. The author believes that a more normal hormone balance can be produced in these cases by the administration of progesterone in cyclic fashion. Experimental evidence indicates that progesterone can influence the secretion of gonadotrophins in animals, but biological assay methods in the human female are not yet available.

In patients under 35 years of age the procedure is to

give 25 mg. of progesterone intramuscularly as soon as the diagnosis of anovulatory bleeding is established by endometrial biopsy. Subsequently regular cyclic bleeding can be induced by administration of progesterone on the 24th day of the cycle. Ovulation was produced in 19 of the author's cases after an interval of 1 to 6 months. In 12 of these cases the anovulatory bleeding was primary (no previous regular cyclic bleeding), and in 7 cases it was secondary (previous regular menstrual periods).

In women over the age of 35, where anovulatory bleeding resulted from failing ovarian function, prolonged bleeding episodes could be prevented by the administration of 25 mg. of progesterone given at 30-day intervals. This might be continued until ovarian production of oestrogen ceases at the menopause.

Profuse bleeding with ovulatory cycles is a more difficult problem occasionally due to the presence of a heparin-like substance in the blood. After excluding organic disease, some of these patients will be benefited by 200 mg. daily of toluidine blue during the menstrual period. The protamine titration test will pick out these cases but the long-term effect of treatment has not yet been evaluated.

D. W. James

43. **The Menopause.**

By E. R. Novak. *J. Amer. med. Ass.*, **156,** 575–578. Oct. 9, 1954.

This paper comes from the Johns Hopkins Hospital. Any discussion on the management of the menopause requires at least a fundamental knowledge of psychosomatics to explain many of the subjective phenomena seen in women at this period. The theme of this essay is that every woman must accept physiological adjustment to cessation of ovarian function, and that protracted continuous oestrogen administration only postpones the adjustment. The only symptoms requiring oestrogen therapy are those relating to the vasomotor system and these are likely to be associated only with scanty menses or amenorrhoea. Intermenstrual bleeding and menorrhagia call for investigation and should not be construed as due to the menopause. Small decreasing doses of oestrogens rarely cause uterine bleeding if given only for short periods.

Androgen therapy is reserved for those cases in which oestrogen might activate a lesion which had become quiescent, such as endometriosis, and for cases where there is a history of carcinoma. Alpha tocopherol as an alternative has given rather equivocal results. Combined oestrogen-androgen preparations may be used, but whatever hormone therapy is employed, and the author's preference is for decreasing doses of oestrogen, it should be used only as a last resort. In all cases adequate explanation and discussion with the patient of the mechanism of the menopause is essential, and in many cases this is the only necessary treatment.

D. W. James

44. **Artificial Insemination at Home.**

By F. E. Lane. *Fertil. and Steril.*, **5,** 372–373. July–Aug. 1954. 1 fig.

It is by no means uncommon for the consultant to be questioned about the detail of artificial insemination (A.I.H.) The author describes and illustrates an easy method which consists in fitting over the cervix of the patient at or about the time of ovulation, a sterile plastic cap to which is attached a length of polythene tubing which either by passing through it or over its rim can be secured to the cap with silk or cotton. When the basal temperature chart indicates ovulation the semen obtained by masturbation is injected at once into the polythene tubing which projects at the vulva. The patient remains lying down for a few hours and the cap is removed. If need be the procedure is repeated on the following day by the husband. Dr. Lane feels that this technique is more acceptable to the suitable case than other methods. Sometimes he states coitus interruptus is a better way of obtaining a specimen from the husband.

V. B. Green-Armytage

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

45. **Treatment of Tumours of the Pelvic Cavity with Supervoltage Radiation.**

By J. G. Trump, R. C. Granke, K. A. Wright, W. W. Evans, H. F. Hare, E. E. Ewert and W. L. Conlon. *Amer. J. Roentgenol.*, **72,** 284–292. Aug. 1954. 2 tables. 7 refs.

Roentgen therapy of tumours of the pelvic cavity, such as cancer of the uterine cervix and urinary bladder, has been among the more difficult problems both clinically and technically. Stage I tumours of the cervix are relatively well controlled by interstitial and intracavitary radium with results as favourable as those from surgery. The percentage of success falls rapidly to about 50 per cent in stage II cases, to about 26 per cent in stage III and to just under 5 per cent in stage IV. Thus the need for the delivery of an adequate dosage throughout the true pelvis is manifest and the authors have tried to do this by utilizing a 2 mev. constant potential radiation to include not only the primary lesion but also the adjacent lymphatics and cellular tissue lying within the confines of the true pelvis as high as the sacral promontory. The intention is to irradiate a volume of a generally spherical shape centred in the pelvis by treating the patient in the standing position which rotates while being exposed to a horizontal circular roentgen beam. Special adjustments, including the placing of a suitable absorber, are carried out to protect the rectum and an effort is made to minimize the dose sustained by the small intestine by the application of an abdominal binder with the patient in the Trendelenberg position prior to irradiation. The roentgen-ray source is a compressed gas insulated Van de Graaf accelerator contained in a steel tank about 3 feet in diameter by 6 feet in overall length. The beam is defined by a variety of adjustable lead and steel diaphragms and apertures so that any rectangular or circular, as well as many complex-shaped, fields can be obtained. The "target to axis of rotation distance" is 125 cm. and it is most convenient to maintain the beam stationary while rotating the patient upon a special

vertical table which provides the required support. Dose distribution within the pelvis is determined by photometric analysis making use of phantoms of anatomical shape. A uniform tumour dose is delivered throughout the pelvis with intensity diminishing from the edge of the selected field so that the dose sustained in the region of the femoral head is about 45 per cent of the axis tissue dose. However, ionization energy absorbed by bone traversed by gamma radiation is only about one-half of that which would be taken up locally from a 200 kv. beam of corresponding intensity. The treatment plan comprises a tumour dose of 6,000 roentgens given in 35 sessions spread over 6 weeks at about 170 r per treatment. The field shape has commonly been a 12–14 cm. circle trimmed at the sides to a 10–12 cm. width just sufficient to lie within the bony pelvis. The rotational administration of such a dose in a typical case delivers a total body dose of approximately 20 million gram roentgens and a tumour dose of approximately 6 million gram roentgens. Most patients have tolerated this treatment well, there being only a moderate post-irradiation reaction and in no case any significant change in the haematological picture. The number of cases of cancer of the cervix treated by this method is small, only about 25, but the results, although relatively recent, appear very promising so far.

J. H. Mulvany

46. **Diagnosis of Cause of Ascites by Study of Cell Nuclei.** (Il metodo cariologico nella diagnosi dei versamenti di natura neoplastica.)

By P. FELETIG. *Minerva ginec.* (*Torino*), **6**, 629–635. Sept. 30, 1954. 10 figs. 25 refs.

The author describes a method of fixing and staining cells from ascitic fluid obtained from cases of abdominal and pelvic carcinoma invading the peritoneum and from cases of ascites due to inflammatory causes and to transudation. Whilst the method cannot give an exact classification of the cellular elements such as can be obtained by Papanicolaou's technique of polychromatic staining, it gives a very reliable answer as to whether the fluid owes its origin to a malignant or non-malignant disease. He points out, however, that a malignant growth not invading the peritoneum can give rise to a static (transudatory) ascites.

His method depends on studying the karyokinesis of the cell nuclei stained with acetic carmine. The steps are (1) immediate centrifuging of the ascitic fluid in two or more containers, (2) collecting the resulting deposits and adding a considerable amount of acetic fixative, (3) a few hours later, recentrifugalize, (4) pipette off the fixing fluid and add a drop or two of acetic carmine to the deposit, (5) after two hours make a slide of a smear of this stained deposit. By this means the structure of the cell nuclei can readily be seen and the frequency of mitosis, whether typical or atypical, observed.

A table of 19 cases of abdominal ascites is given showing that a correct diagnosis (malignant or non-malignant) was made in every case by this method. The author naturally remarks that, so far as malignancy is concerned, a positive diagnosis is of little help from the clinical point of view as the disease must already have reached an advanced stage. The article is illustrated by some interesting slides.

W. C. Spackman

47. **Results of a Planned Attack on Carcinoma of the Vulva.**

By S. WAY. *Brit. med. J.*, **2**, 780–782. Oct. 2, 1954. 6 figs. 4 refs.

In 1941 the author described an extended radical vulvectomy and node dissection which involved removing a wide area of skin and the regional glands as far as the bifurcation of the common iliac artery. From 1943 onwards, an experiment was tried in which all cases of vulval carcinoma in the Newcastle area were referred to him and he carried out radical surgery whenever possible. Between then and 1949, 79 cases were seen and this paper reviews the 5-year follow-up results.

The operability rate was 83 per cent and it appears that it might be even higher in the future if more of the very old and diabetic patients were dealt with by staged operations. Tumour size and involvement of urethra, vagina or rectum were not regarded as contra-indications to radical surgery nor was node involvement per se. Rejection was almost always decided on a combination of advanced tumour, advanced age and concomitant disease. One patient refused treatment.

The absolute 5-year cure of all cases seen was 61 per cent, and 74 per cent of those operated upon were alive and well. In 32 per cent of cases, the nodes were involved and of these 48 per cent survived. Eighty-six per cent of the 44 cases without node involvement were alive and well at 5 years.

Anatomical spread of the cancer to the lymphatics is fairly regular and involvement of the deep nodes only occurs in about 15 per cent of cases. After determining this fact, since 1952 the author, with the cooperation of Dr. Ruth Dearing, has modified his original technique. He now exposes the external iliac nodes and removes the lowest medial and the lowest lateral ones. These are smeared and stained in a few minutes while the superficial glands are being removed. If the deep nodes are not involved, the inguinal ligament is not divided and no further iliac dissection is undertaken. If they are involved, the earlier technique is followed.

Wide excision of the vulval area appears to be the greatest advance in treatment for there was no local recurrence up to 5 years in this series. Teamwork at a special centre is essential for the best results.

Doreen Daley

48. **Prognosis in Cancer of the Uterine Cervix Based on the Vaginal Smear Before Treatment: SR—the Sensitization Response.**

By J. B. GRAHAM, R. M. GRAHAM and W. LIU. *Surg. Gynec. Obstet.*, **99**, 555–562. Nov. 1954. 10 figs. 4 refs.

Some patients with cancer of the cervix exhibit cells in the vaginal smear that are unlike those in the normal. The alteration is a cytoplasm that is finely vacuolated and simultaneously increased in density. It stains a deep

lavender with Papanicolaou's polychrome stain. These changes are principally found in the basal cells but occasionally in the precornified cells as well. It is called the sensitization response, or SR, because when present the tumour and the patient are usually sensitive to irradiation.

In some patients SR is prominent; in others it is absent. A quantitative estimate is arrived at by differentially counting 100 consecutive non-malignant epithelial cells. The number of cells showing SR is expressed as a percentage. Patients whose smears showed 10 per cent or more of the cells with SR are said to have marked SR. Those in whom no more than 9 per cent of the benign epithelial cells show SR are classified as poor SR.

The authors present from Boston, Massachusetts, a series of 136 patients treated radiologically and 103 patients treated surgically.

Of the 136 treated radiologically, 51 had marked SR and 37 (73 per cent) of these survived 5 years. Of the 85 patients with poor SR only 15 (18 per cent) survived a similar period.

Though poor SR is associated with a poor prognosis in Stage I and II lesions treated radiologically, quite the opposite—a good prognosis—is found if lesions of the same extent with poor SR are treated surgically. Of 80 patients with poor SR, in whom a radical hysterectomy was done, 57, or 71 per cent, survived for from 2 to 5 years. In contrast, of 58 patients with poor SR treated with radiation, only 14, or 24 per cent, survived 5 years. This suggests that the patient with poor SR and a Stage I or II cancer of the cervix would be better treated surgically than by radiation.

How well do patients with marked SR do if treated surgically? The survival rate is roughly half that of the radiated cases. Twenty-three patients with good SR had radical hysterectomies and 9 survived, 39 per cent. This would appear to indicate that, for the Stage I and II patient with marked SR cytologically, the treatment of choice is radiation rather than radical surgery.

It is noted that SR has prognostic significance only if the form of treatment is considered. If the survival rate of all cases with marked SR is compared with the survival rate of all cases with no SR without taking into consideration the type of therapy, there is no difference.

SR requires a certain amount of special training and knowledge of cytology that is not generally available. A cheaper method that could be done by those without any training was sought in the basal cell counts. Although basal cell incidence lacked the precision of SR in prognosis, it showed the same general trend as SR in both series, thus supporting the different outlook depending upon the mode of treatment.

The authors conclude that SR is a useful prognostic index in patients with cancer of the cervix and that it may serve in the selection of the appropriate form of treatment. The estimation of SR is a technique which can be taught and learned in a reasonable period of time. The proportion of basal cells is of limited prognostic value but follows the same general trend as SR.

John P. Erskine

49. **Radio Resistant Cervical Cancer.**

By E. R. Novak, *Obstet. Gynec.*, **4**, 251–259. Sept. 1954. 6 figs. 17 refs.

The generally accepted treatment for cervical malignancy consists of irradiation alone or various combinations of radium and deep X-ray therapy, with routine surgery reserved for only the intra-epithelial lesions. The author does not agree with the routine of irradiation followed by surgery, considering that the incidence of such complications as fistulas is high in the freshly irradiated patient. Of even more importance is the tendency for operation to disseminate viable cancer cells which have been walled off by irradiation. A few large hospital centres with unusual facilities and expert surgeons can offer radical surgery to selected patients, but the 5-year salvage is not distinctly higher than that achieved by well-planned irradiation therapy. If there is involvement of lymph nodes, lymphadenectomy will cure only a few cases. However, if a patient has received adequate radiation and the cervical lesion is still active, surgery represents the only hope for salvage.

Most types of cervical cancer are radiosensitive (which must be distinguished from radiocurable). If viable tumour is found at biopsy 6 to 8 weeks after radiotherapy, treatment can be said to have failed. Generally, the more highly differentiated lesions, while less invasive, are more refractory to irradiation, although Glücksmann and Spear and others do not agree.

From a study of 450 cases of cervical cancer the author is convinced that the clinical stage of the disease is the only important prognostic factor. No correlation was found between tumour behaviour from biopsies and prognosis. In the author's clinic radical surgery was used for recurrent or early radioresistant cases. After discarding recurrences later than one year, there were only 12 patients who were adequately irradiated but continued to have active cancer. Ten of these showed a well differentiated tumour. Each case is described in the author's article. He concludes that satisfactory correlation of radiation effect and clinical course is not practical, there being too many variables. Amongst the latter is a patchy localized response to irradiation which indicates that random biopsy will not give an accurate picture of tumour behaviour.

J. G. Dumoulin

50. **Transvaginal Roentgen Therapy in Cancer of the Cervical Stump.**

By R. M. Caulk. *Amer. J. Roentgenol.*, **72**, 469–473. Sept. 1954. 4 tables. 17 refs. Discussion.

Cancer in the cervical stump occurring later than a 2-year period after supracervical hysterectomy may be estimated to be a new development unrelated to the state of cervical pathology at the time of operation. The incidence of cancer of the cervical stump present, but overlooked, at the time of operation was found to be 27 per cent in 781 collected cases of carcinoma of the cervix after subtotal hysterectomy, a circumstance which advocates strongly the removal of the cervix in all cases of hysterectomy.

Difficulty in treating cancer of the cervical stump with

radium is mainly due to the absence of an adequate cervical canal and the author has developed (*Radiology*, 1949, **52**, 37) a form of transvaginal roentgen therapy which gives a wide field of exposure and appears to be more effective than other methods. Twenty-five cases have been treated by this method and 16 have survived over a 5-year period, giving a percentage of 64. Three of this group were stage III cases, all of whom died, so that the rate of cure for stages I and II was approximately 72 per cent. The overall cure-rate of 64 per cent, however, may be compared with a general average of about 40 per cent although the Radium Centre, Jutland, in a small group of 12 cases obtained 7 survivals, an incidence of 60 per cent. In addition to greater effectiveness, it was also noted that the degree and incidence of vaginal atresia was materially lessened.

J. H. Mulvany

51. Interstitial Radium Treatment of Cancer of the Cervix Uteri.

By J. A. CORSCADEN, S. B. GUSBERG and W. KOSAR. *Amer. J. Roentgenol.*, **72**, 278–283. Aug. 1954. 2 tables. 5 refs.

A report of a trial of the interstitial technique of radium therapy in the treatment of 108 cases of cancer of the cervix is made. It is considered that the method has advantage over the intracavitary technique in being able to deliver a more efficient dosage to the lateral pelvis and to avoid the injurious effect of external radiation to superficial structures. The intention was to irradiate not only the area where the tumour was apparent, but also those spaces accessible to implantation where cancer spread might take place. An intra-uterine tandem containing 20–30 mg. radium is inserted, followed by the interstitial implantation of the needles in the form of a stockade around the cervical canal, eight 1·5 cm. needles, each containing 1·98 mg. radium, being inserted into the cervix about 1 cm. apart. The parametrial allocation consists of two of the above type of needles inserted on each side of the cervix at 3 cm. distance from it and that of the lateral pelvic wall of 5 needles, each containing 5 mg. radium, placed in the sagittal plane at a distance of 4–5 cm. from the cervix. The whole would be left for 120 hours. In practice, however, the application was seldom ideal owing to technical difficulty, such as might be caused by narrowness of the vagina or obliteration of the cervical canal, or to excessive caution on the part of the operator. Surgical injury was uncommon and post-irradiation sequelae relatively unimportant, apart from one case of rectovaginal fistula for which a colostomy was required, and one instance of vaginal ulcer which gave rise to profuse bleeding 5 months later when a further application of radium given in a pack led to uraemia from ureteral blockage by oedema. Experience has shown that irradiation effects can be lessened by reducing the strength of the radium in the tubes notwithstanding a lengthening of the duration of the application. Thus, by reducing the dosage of the intra-uterine tandem to 15 mg. and that of the needles in the cervical insertion to 1 mg., the dose to the cervix would be lowered from 26,000 r gamma to 18,000 r gamma, while the dose maintained at a point 3 cm. lateral to the internal os would still be 12,000 r gamma. In some cases of proctitis, the wide area of bowel affected suggested that external irradiation might have been the major factor causing it. The principal cause of error in the technique of radium insertion has been inattention to the accurate placing of the needles. The results obtained were considered to be superior to those formerly achieved by the intracavitary technique. Thus, of 22 stage II cases, 50 per cent were alive and well after more than 5 years. In stage III, the results were poor but still considered to be greatly superior to those obtained by the older method. The numbers treated are too small to have statistical significance but the results nevertheless show considerable promise.

J. H. Mulvany

52. The Management of Ovarian Tumours.

By K. T. MACFARLANE. *Canad. med. Ass. J.*, **71**, 440–444. Nov. 1954. 2 tables. 9 refs.

Pathological examination of 1,731 specimens of ovarian tumours from the Gynaecological Service of the Montreal General Hospital from 1933 to 1952 revealed 1,191 or 90·9 per cent to be of benign nature. Excluding non-neoplastic ovarian enlargements, 540 proliferative tumours were reviewed, 383 (70·9 per cent) being benign, 157 (29·1 per cent) malignant.

The management of ovarian enlargements is dependent upon multiple factors. Tenderness suggests a benign mass of inflammatory or endometrial origin or undergoing torsion or rupture. A cystic mass of 5·0 cm. may be watched, while one of 5·0 cm. or more, showing increase in size, or discovered after the menopause, requires immediate removal, as does the solid mass. At operation physiological cysts are preferably treated by puncture and dermoids and endometrial cysts by excision in younger women, whereas proliferative tumours (cystadenomata) require oöphorectomy, especially where the other ovary proves to be normal. The presence of papillary excrescences suggests a serous, potentially malignant cyst, requiring frozen section and careful examination of the remaining ovary (even bisection) if less than bilateral oöphorectomy is to be done.

The principal generalizations about malignant tumours are well known, most tumours appearing after the menopause, usually of asymptomatic progression until wide extension has occurred. The most effective treatment is complete surgical removal, complete abdominal hysterectomy with bilateral salpingo-oöphorectomy. The author does not use post-operative irradiation where complete and apparently clean removal of the tumour has been possible, but believes irradiation may increase the survival rate in cases of incomplete removal without spread to the upper abdomen.

Means of prevention or early detection are discussed, namely routine 6- to 12-month gynaecological examination of women over 40 years of age, prophylactic removal of ovarian tissue at pelvic operation in women of 45 years and over, or past the menopause, or in radical treatment of chronic pelvic inflammatory disease or endometriosis, and correct assessment of the small ovarian mass.

Limiting the search for genital cancer to the Papanicolaou cytological test is not advocated. The place for pelvic examination under anaesthesia is discussed.

O. Schmidt

53. **Primary and Secondary Ovarian Adeno-acanthoma.** By M. B. DOCKERTY. *Surg. Gynec. Obstet.*, **99**, 392–400. Oct. 1954. 7 figs. 7 refs.

This is a report from the Mayo Clinic of 40 cases of ovarian adeno-acanthoma discovered in a group of some 2,000 ovarian tumours, an incidence of 2 per cent.

In 13 instances the tumours were designated as primary as there was unquestionable evidence that the lesions arose in ovarian tissue. In the remaining 27, or secondary group, endometrial involvement was present or could not be excluded so that the ovarian tumours might have been either metastatic or independent primary neoplasms.

The salient clinical features common to both groups were an average age considerably less than that reported for patients with ovarian cancers in general, and a somewhat reduced incidence of fertility. The association of endometrial carcinoma gave a high incidence of abnormal bleeding among patients with lesions in the secondary group, but in most other respects no outstanding differences were observed.

Treatment, whenever possible, was by total hysterectomy and bilateral salpingo-oöphorectomy followed by deep X-ray therapy. In the primary group 7 of the 13 patients were alive and well for periods of 5 to 24 years. In the secondary group follow-up was possible in 18 instances and of these 9, or 50 per cent, had survived for at least 5 years and were free from carcinoma.

Without a doubt certain of the ovarian lesions in the secondary group were truly metastatic. However, the fact that many of the endometrial foci were small and resembled implants, coupled with the surprisingly good 5-year survival rate for patients with combined endometrial and ovarian lesions, gives strength to the author's belief that this strange combination frequently represents the development of separate primary growths.

The tumours had no macroscopic features to make differentiation possible from other ovarian carcinomas. Histologically they were very reminiscent of endometrial carcinoma. The high incidence of associated pelvic endometriosis and the frequent finding of benign areas within the tumours, increased the likelihood that many did originate in ectopic endometrium.

John P. Erskine

54. **Conservatism in Endometriosis.** By J. I. BREWER and F. M. MAHER. *Amer. J. Obstet. Gynec.*, **68**, 549–558. Aug. 1954. 3 figs. 23 refs.

The most frequent reason for failure to diagnose endometriosis is neglect of vaginal and rectal palpation of the posterior cul de sac and utero-sacral ligaments. Dysmenorrhoea may be relieved by daily oral doses of oestrogens for 6 days before ovulation. More persistent and severe pelvic pain may be controlled by daily doses of 10 to 100 mg. of diethylstilboestrol. Such therapy should not continue for longer than 3 months. Androgens in doses of up to 200 mg. a month have been used with good results but oestrogens are just as effective, and are less prone to cause unpleasant side effects. Abnormal uterine bleeding can also be relieved by large daily doses of oestrogens. With such therapy it is possible to postpone operations for a considerable length of time in young patients, and during this time many will become pregnant.

Conservative surgery seeks to relieve symptoms without interfering with future childbearing. In many cases endometrial ovarian cysts can be enucleated with ease, leaving the entire capsule of the ovary with all the functional elements. It is, however, doubtful if operations simply to increase fertility, in absence of symptoms, are justified.

When operations are performed for endometriosis, or when endometriosis is encountered during an abdominal operation, approximately one-third of the patients will subsequently conceive if conservative procedures are adopted and if there is no other cause for sterility.

F. J. Browne

OPERATIONS

55. **Hysterectomy and Undiagnosed Pregnancy.** By S. T. DELEE. *West. J. Surg. Obstet. Gynec.*, **62**, 553–556. Nov. 1954. 1 ref.

The need for accurate diagnosis before hysterectomy is stressed and the author advocates the use of biological tests, pregnanediol excretion assay, vaginal smears or the Schiller iodine test before starting to operate on a woman during the reproductive era. If the abdomen has been opened and the presence of a pregnancy suspected, the blue hue and soggy consistency of the uterus may lead to the correct diagnosis. The injection of 0·5 ml. pituitrin into the pregnant uterus causes rhythmical contractions and blanching round the site of injection; with fibroids, etc., there are no contractions and only very local blanching. If real doubt is experienced, amniotic puncture with a fine-bore needle is safe or the uterus may be carefully incised to try and expose the amniotic sac. The appearance of a corpus luteum in the ovary is not a reliable guide.

D. C. A. Bevis

56. **Prolapse Following Hysterectomy.** (Les prolapsus génitaux après hystérectomie.) By E. POLLOSSON and J. MATHIEU. *Gynéc. Obstét.*, **54**, 289–295. 1954.

The types of prolapse which can appear following hysterectomy, whether it be total, subtotal, or vaginal, produce different curative problems, which can be solved in different ways. An investigation into the French literature of the last few years reveals little or nothing, but the American publications on this subject are numerous and opinions very divergent.

Fifty-four cases are reported on: 32 followed subtotal hysterectomy chiefly for fibroids, 15 followed total hysterectomy and only 5 followed vaginal. Two cases followed after very high amputation of the cervix and 1 after unspecified abdominal hysterectomy.

It seemed reasonable to the writers to exclude in their

paper those patients with fibroids who had at the same time vaginal prolapse and in which the hysterectomy had aggravated the degree of prolapse.

In 48 patients, in whom real details of the type of prolapse were available, 20 showed cystocele only and rectocele was the main lesion in 8. Deficiencies of both anterior and posterior wall were noted in 20 cases.

As regards treatment, 16 were not submitted to operation owing to their general condition of age, diabetes, hypertension, etc. In these pessaries were used. Five of these were total hysterectomy cases: 9 subtotal and 1 vaginal.

In several cases, after the administration of synthetic oestrogens, considerable improvement of the state of the vaginal walls followed.

Thirty-nine were treated surgically: 17 by vaginal obliteration according to Lefort's technique, 7 by vaginal obliteration according to La Barthe's technique, 10 by anterior and posterior colporrhaphy, 1 by amputation of the cervix and repair of the perineum, 1 by posterior colporrhaphy only, 4 by posterior colporrhaphy plus Marion's operation for stress incontinence.

Seventy-five per cent had eminently satisfactory results.

D. Maxwell

57. **Plastic Surgery of Closed Tubes with Chorion-Amnion.**

By B. S. Ten Berge and The Tik Lok. *Fertil. and Steril.*, **5**, 339–352. July–Aug. 1954. 15 figs. 1 ref.

The authors describe the use of this material in considerable detail but their experience is that of the reviewer who for a matter of 2 years used this material which takes much time and trouble to prepare. It gives no better results. Indeed, perhaps worse results than other methods, for although, may be, the tubes are left patent, the mosquito-curtain-like membrane by obscuring the fimbrial ends prevents entry of the ovum. The authors have recorded no successes after 6 patients had been treated with amnion.

V. B. Green-Armytage

58. **Reconstruction of Fallopian Tubes by Vein and Artery Implants.**

By A. M. Davids and A. Bellwin. *Fertil. and Steril.*, **5**, 325–333. July-Aug. 1954. 2 figs. 20 refs.

The authors are advocating the above transplants for cases of chronic salpingitis which have resulted in hydrosalpinx, and they do this by splitting what remains of the tube longitudinally and then implanting a 4–6 inch portion of the patient's vein or artery and sewing over them. They do not make plain how the chronically inflamed tube retains the vein or artery without a recrudescence of inflammation, though they recommend the use of a reamer at the cornual angle.

[The vein they use is the saphenous but it is difficult to foresee how such an implant can retain its normal health and structure when laid in a bed of the cut edges of the broad ligament or in the lumen of a diseased tube, though they do suggest the use of polythene tubing. One's experience of the health and welfare of any transplant leads one to conclude that it solely depends upon an efficient mesenteric border of blood vessels, and so although the idea is pleasing it is difficult to foresee how the wall and endothelium of a 4-inch portion of the saphenous vein nakedly stretching from the cornu to the ovary is going to receive sufficient new vascular nurture to survive, although such a method in the female dog as described by the authors suggests the possibility of success. But in such a case no previous disease exists.]

V. B. Green-Armytage

59. **The Polythene Catheter in Tubal Occlusion. Report of 8 Cases.**

By B. Rubio, L. *Fertil. and Steril.*, **4**, 233–235. May–June 1953. 14 refs.

During the last few years diverse materials have been tried to obtain post-operative tubal patency, though there is little question that fair results can be obtained by simple anchorage of the implantable portion of a tube into the cornu either by a coronal incision or through an adequate tunnel. Since there is always the risk of subsequent stenosis, many have advocated the use of silver or tantalum wire, chromic catgut, ureteric catheters, and more recently polythene tubing. The latter offers an advantage over other methods in being completely inert, antioxidant free, and causing no tissue reaction. The author reports 8 patients who after investigation by hysterogram and CO_2 underwent tubo-uterine implantation, the tubing being removed after 6 or 7 weeks. [We feel that there is considerable danger in the use of tubing for organisms and septic material can pass up the tube from the vagina by capillary attraction giving rise to subsequent occlusion, either at the fimbrial ends or at the internal ostium. For this reason we advocate the use of solid rods of polythene (PTFE) rather than tubing. It is easier to thread through the tube and it passes readily through the uterus into the vagina as it is less flaccid than hollow polythene. The solid size we advocate is 1·2 mm. in diameter.] Dr. Rubio reports that post-operative tubal patency was present in 7 cases out of 8. Two patients conceived after operation, 2 and 3 months later respectively. There can be little doubt that this operation can give the greatest satisfaction to those who will do it, for, if surgeons today can get a 25–30 per cent success rate in patients who otherwise would be doomed to permanent sterility, conjugal infelicity or divorce, it is certain that with growing experience their results will be commensurately greater.

V. B. Green-Armytage

60. **Salpingostomy: Treatment of Female Sterility.**

By A. C. Comninos. *Fertil. and Steril.*, **5**, 334–338. July–Aug. 1954.

The author stresses the fact that 50 per cent of all tubal occlusions are permanent and that no conservative or medical treatment such as was once advised is of the least use. Therefore, whenever possible operation is the only chance, though the prognosis is very poor in cases where there is any distension or thickening of the tube with or without peritubal adhesions. He records 148 cases of salpingostomy, of which 65 per cent were in patients with primary sterility. They were all investigated

by hystero-salpingography and Rubin's test. The operative technique was the same as used here, that is the making of a new ostium followed by slight eversion of both lips with fine atraumatic catgut sutures, the instruments all being ophthalmological ones. The author stresses the importance of always ventro-suspending the uterus afterwards and of doing a hystero-salpingogram on the 9th post-operative day, which he considers helps in the maintenance of patency of the newly reconstructed ostium. He found, as we have found here, considerable difficulty in following up such patients post-operatively, but, out of 37 patients who reported, he had a total of 14 tubal patencies, and 6 of these conceived after operation, that is 16 per cent. There was 1 ectopic. He considers that, with extended practice and the ability to operate on these cases, future results will be far better.

V. B. Green-Armytage

61. **Uterotubal Insufflation. Value in the Treatment of Tubal Obstruction to Ovular Migration.**

By I. C. RUBIN. *Fertil. and Steril.*, **5**, 311–324. July–Aug. 1954. 7 figs. 15 refs.

As the human ovum measures 100 microns in the follicle and 150 microns in the Fallopian tubes, it is obvious that its transference to the uterine cavity depends upon there being no stricture or bend or spasm that would reduce the narrowest portion of the duct below 150 microns in diameter. Rubin points out that spasm is one of the commonest causes of high readings during insufflation and that they can be reduced (1) not only by antispasmodics such as octyl nitrite, but by avoiding the use of cold cannulae and the rough passage thereof. (2) By not applying a tenaculum to the whole thickness of the anterior lip of the cervix; and (3) by maintaining the maximum pressure for at least 2 minutes. He insists that there is no question whatever that moderate tubal obstructions of an organic nature can be improved by insufflation, and points out that his pregnancy success rate for patients who have been proven by high pressures to have such slight obstruction is 18·6 per cent; whereas 26 per cent of women with normal tubal pressures in his practice conceived. For these reasons he advocates repeated uterotubal insufflation where obstruction has been previously demonstrated and goes on to state that the total number of pregnancies in his practice which were preceded by pressures greater than 100 mm. Hg on one or more occasions was 46·4 per cent.

V. B. Green-Armytage

62. **The Interpretation of the Oscillations of Kymograph Tracings during Utero-tubal Insufflation.** (Interprétation des oscillations enregistrées au cours de l'insufflation utéro-tubaire kymographique.)

By L. BONNET. *Gynéc. Obstét.*, **53**, 491–498. 1954. 2 figs.

Up to 1941 the tubal origin of the oscillations of the kymograph tracing registered during utero-tubal insufflation was never questioned, but at that time Stabile, with several followers, questioned that the origin might be uterine.

The author, after analyzing the experiments of Rubin and Stabile, also his own, developed his arguments and finally published his results at the New York International Conference of Fertility and Sterility in 1953. They were very briefly as follows:

1. The oscillations registered clinically are caused by the rhythmic stopping of the flow of the gas in the tubes.
2. These cessations of rhythmic flow are produced at the narrow junction of the interstitial and isthmic portions of the tube, as a result of rhythmic contractions of a more or less long segment of muscular section of the tube at that point.
3. Under these circumstances and assuming that the medial portion of the interstitial section of the tube represents a mixed zone, where the uterine and tubal fibres fuse, then the oscillations with the type of machine in common use represent tubal contractions and do not represent a hysterogram.

D. Maxwell

UROLOGY

63. **The Results of Chemotherapy in Urinary Infections.**

By L. P. GARROD. R. A. SHOOTER and M. P. CURWEN. *Brit. med. J.*, **2**, 1003–1008. Oct. 30, 1954. 4 refs.

For one year, a controlled investigation of the prophylactic use of 1 g. of "sulphatriad" three times daily for 7 days after vaginal surgery, was undertaken. Two wards took part in the trial, alternating between this chemotherapy and no drug prophylaxis each three months. The urine was cultured just before operation and on the 10th day afterwards, unless an earlier test was indicated clinically. Pre-operative infection was found in only 6 of 113 cases. Most cases had a self-retaining catheter for about 4 days and continuous drainage was more often employed than a spigot.

Infection occurred in the majority of cases in both treated and untreated groups, only 15 per cent of the former and 7 per cent of the latter escaping it. Analysis of the figures suggested that patients with no indwelling catheter did a little better than those not so treated but only 17 women had no indwelling catheter and of these 6 did not need catheterization at all, 5 of them remaining free from infection.

Str. faecalis infections were relatively more frequent and coliform infection less frequent in the sulphatriad group than in the controls.

Doreen Daley

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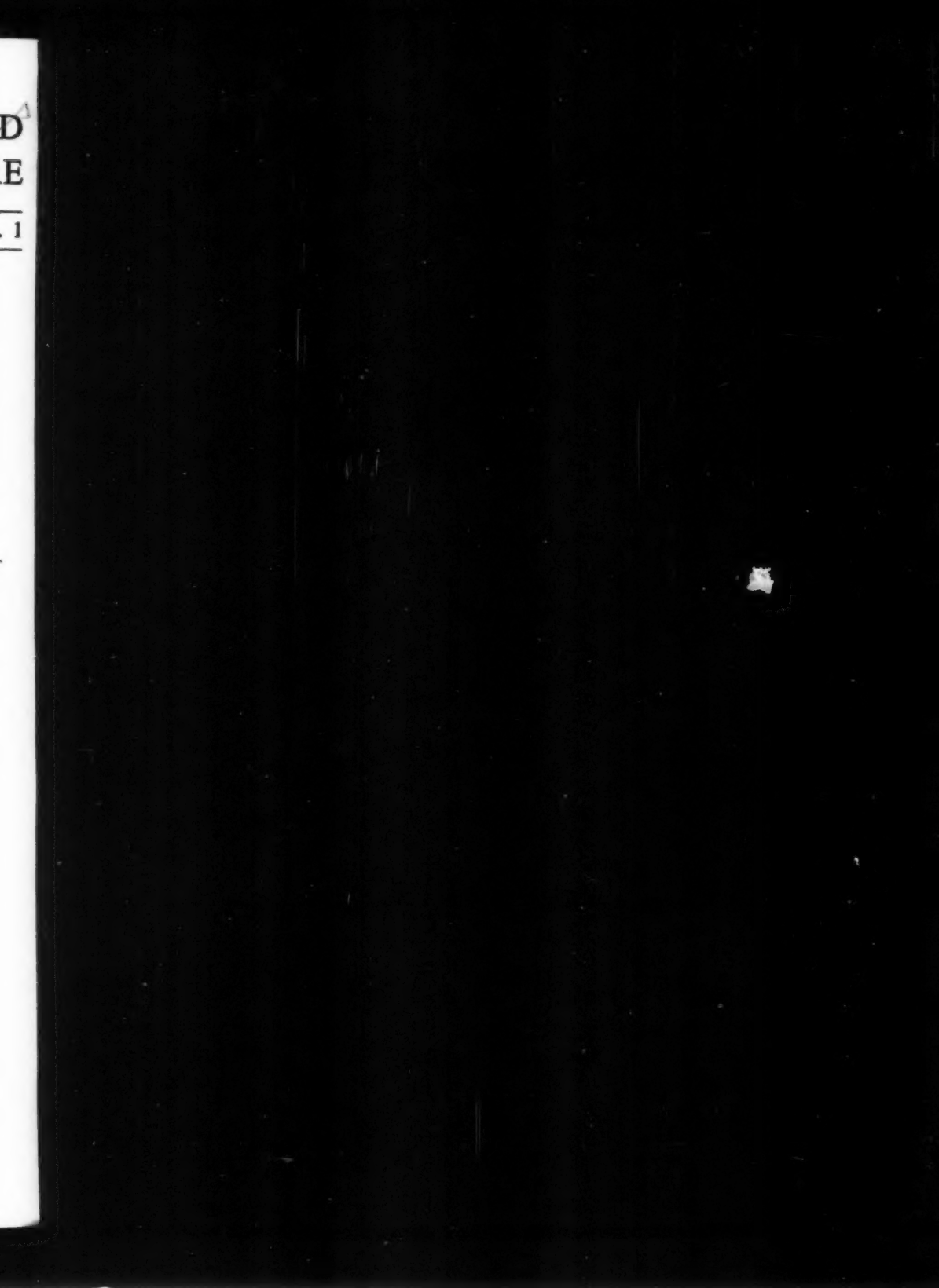
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